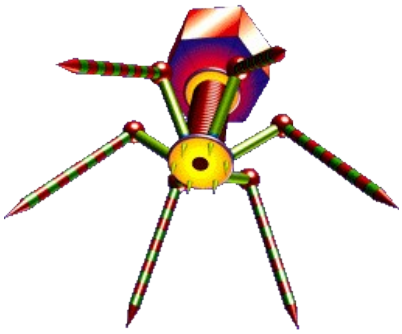

Bacteriophage Ecology Group (BEG) News

Dedicated to the ecology and evolutionary biology of the parasites of unicellular organisms (UOPs)

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January 1, 2000 issue (volume 3)

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Editorial

Editorials should be written on subjects relevant to The Bacteriophage Ecology Group as an organization, to *BEG News* (either the concept or a given issue of *BEG News*), or the science of Bacteriophage Ecology. While my assumption is that I will be writing the bulk of these editorials, I wish to encourage as many people as possible to seek to relieve me of this duty, as often as possible. Additionally, I welcome suggestions of topics that may be addressed. Please address all correspondence to abedon.1@osu.edu or to "Editorials," *Bacteriophage Ecology Group News*, care of Stephen T. Abedon, Department of Microbiology, The Ohio State University, 1680 University Dr., Mansfield, Ohio 44906. Please send all submissions as Microsoft Word documents, if possible (I'll let you know if I have trouble converting any other document formats), and in English.

Bacteriophages as Model Systems

"Ecologists who are not thoroughly familiar with the organisms involved risk wasting a great deal of time."

Nelson G. Hairston, Sr.

For years now I've straddled the divide between the bacteriophage molecular and the bacteriophage ecological, never quite understanding the motivations of those who are dedicated to only one but not the other. The problem as I see it is one of using bacteriophages as model systems. Regardless of one's orientation, such an attitude is degrading to bacteriophages, as it is any individual who is objectified rather than treated as a whole. Take molecular types. With enormous success organisms have been reduced to their component parts, unless there is some economic incentive to do otherwise, with little regard for the subtleties of environmental interactions. The phage has a nucleic acid polymerase, the better to understand polymerases! But who cares where that phage uses that polymerase, nor how many phages it makes with it, much less why.

Purely ecology types are not much better. Sure phage populations do interesting things, and they are so simple that experimentation is far simpler than, say, setting up the Serengeti in the laboratory. Lions, and even zebras, are complex creatures, living in complex environments; so much easier it is to study a simple bacteriophage, infecting a simple bacterium, living together in a simple broth culture. However, simplicity can be deceiving. We only know that lions, zebras and the Serengeti are complex systems because we can see those complexities. As any molecular type could tell you, however, bacteriophages and bacteria (and even broth cultures as the ecology types might retort) can also be pretty darn complex. But it's easy to pretend

otherwise because we can't see these complexities with our own eyes.

The solely molecular types have created a world in which phages are highly complex molecular model systems that have no ecology, while the solely ecological types have created a world in which phages are represented as simple ecological model systems. Obviously both views are quite misleading. And just as obvious, bacteriophage ecology is an irrelevant discipline, and increasingly so, unless it is based on a robust understanding of bacteriophage complexity. Only with such an understanding can one argue that the experimental manipulation of phages is justifiable because robust conclusions are possible only with systems that are understandable. But just because bacteriophages have that potential does not mean that the potential will be realized. Ideally all bacteriophagologists would take a strong interest in both the molecular and the ecological. Minimally, bacteriophage ecologists should never lose site of the molecular (and physiological) complexity of the organisms with which they work.

MicroDude, a.k.a., **Stephen T. Abedon**

Developer and Editor
The Bacteriophage Ecology Group
Dedicated to the ecology and evolutionary biology of the parasites of unicellular organisms (UOPs)

Editorial Archive

- BEG: What we are, Where we are, Where we're going
- When Grown *In Vitro*, do Parasites of Multicellular Organisms (MOPs) become Unicellular Organism Parasites (UOPs)?
- Bacteriophages as Model Systems

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New BEG Members

The BEG members list can be found at beg_members.htm as well as on the BEG home page. As we add new members, these individuals will be introduced in this section. Note that, in fact, there are two ways of "joining" BEG. One, the traditional way, is to have your name listed on the web page and on the list server. The second, the non-traditional way, is to have your name only listed on the list server. The latter I refer to as "non-members" on that list. Members, e.g., individuals listed on the BEG home page, should be limited to individuals who are actively involved in science and who can serve as a phage ecology resource to interested individuals. If you have an interest in phage ecology but no real expertise in the area, then you should join as a non-member. To join as a member, please contact BEG using the following link: abedon.1@osu.edu. Include:

- your name
- your e-mail address
- your snail-mail address
- the URL of your home page (if you have one)
- a statement of whether or not you are the principal investigator
- a statement of your research interests (or phage ecology interests)
- a list of your phage ecology references, if any

Note that it is preferable that you include the full reference, including the abstract if the reference is not already present in the BEG bibliography. Responsibility of members includes keeping the information listed on the BEG members list up to date including supplying on a reasonably timely basis the full references of your new phage ecology publications. Reprints can also be sent to *The Bacteriophage Ecology Group*, care of Stephen T. Abedon, Department of Microbiology, The Ohio State University, 1680 University Dr., Mansfield, Ohio 44906. To join BEG as a non-member, please contact BEG using the following link: abedon.1@osu.edu and minimally include your name and e-mail address.

Please welcome our newest members:

name (home page links)	status	e-mail	address
Eduardo C. Schröder	PI	e_schroder @hotmail.com	BNF Laboratory, P. O. Box 9030, Department of Agronomy and Soils, University of Puerto Rico, Mayagüez, PR 00681-9030 USA
	interests:	Phages specific for Nitrogen Fixing Bacteria (*Azospirillum*, *Bradyrhizobium*, *Rhizobium*, etc.); their ecology, host range and characterization.	
Sung-Sik Yoon	PI	ssyoon @unity.ncsu.edu to 2/28, then sungsik @dragon.yonsei.ac.kr	Department of Biological Resources and Technology, College of Arts and Sciences, Yonsei University, Kangwon-do, Wonju 220-710, South Korea
	interests:	Lactic acid bacteria(LAB) bacteriophages from fermented vegetables which include isolation and characterization, analysis of genetic make-up of holin and endolysin gene, lysogenicity of phage, and phage-resistance mechanisms. Bacteriocins produced from *Leuconostoc* species.	
Sema Akinlar Yuksel	---	sema.yuksel @stir.ac.uk	Institute of Aquaculture, University of Stirling, FK 9 4LA, Stirling/ UK
	interests:	Characterization and detection of the *Rickettsia*-like organisms in fish.	

New Links

Links relevant to The Bacteriophage Ecology Group fall into a number of categories (e.g., see Bacteriophage Ecology Links at beg_links.htm). Listed below are those links that overtly deal with phage ecology issues. With each issue of *BEG News* this list will be included, *in toto*, but updated with new links and with no-longer-working links both clearly indicated. If you know of a link that should be included on this page, or the whereabouts of a now-dead link, please let me know.

- Abundance and variety of bacteriophages
- Algal Virus Workshop (abstracts from June 14-18, 1998 meeting) [new]
- Assessment of MS2 Bacteriophage Adsorption to Koch Membrane
- Bacteriophage Ecology Bibliography
- Bacteriophages (an overview)
- Bdellovibrio [new]
- BioVir Laboratories (an environmental testing laboratory)
- Can Pseudolysogeny be induced by Antibiotics? [new]
- Characterization of Marine Viruses
- Coliphage Field Kit: Technical Final Report (lots of technical info on using coliphages as indicators of fecal contamination)
- The Curious Microbe: *Bdellovibrio*
- Determination of Optimal Conditions for Bacteriophage Lysis of *Janthinobacterium lividum* Broth Cultures
- The Ecology of Computer Viruses
- The effect of phosphate status on virus populations during a mesocosm study
- Host Interactions and Growth Strategy of Aquatic Bacteriophages
- How the cholera bacterium got its virulence
- The Isolation of T-Even Phages
- *Lactococcus garvieae* Phage
- The Microbe Zoo | Dirtland | House of Horrors [featuring the strangler fungus, *Vampirococcus* and *Bdellovibrio*]
- Marine bacteriophage reproduction under nutrient-limited growth of host bacteria. I. Investigations with six phage-host systems [new]
- Molecular Bacterial Ecology Group
- Molecular ecology and evolution of *Streptococcus thermophilus* bacteriophages in industrial milk fermentations
- MS2 Inactivation by Chlorine during Microgravity
- Phage (an introduction to some basic phage biology)
- PhageBiotics Foundation
- Phage-Tech Interest Group [new]
- Pseudolysogeny
- Revenge of the Bug Zappers
- A Review of the ASCRC Starter Strategy
- Toward a Theory of Molecular Computing (includes Lambda-Phage Choice Between Lysis and Lysogeny Model)
- Transgenic Transgression of Species Integrity and Species Boundaries (a review) [new]

New Features

In this section I will highlight new or updated features of the BEG site. If you have any ideas of how either the BEG site or *BEG News* might be improved, please let me know.

sta0001.htm is (almost) no more:

This page had been the Bacteriophage Ecology Group main/home page. Two things motivated this change. One was a complaint that this page was taking longer and longer to load. The second was that I am slowly attempting to make the file names on the site more meaningful (well, have meaning, period). All of the material that was formerly found only on sta0001.htm can still be reached via the Bacteriophage Ecology Group splash (now also home) page: www.phage.org. The new file names include: "beg_mission_statement.htm," "beg_members.htm," "beg_bibliography.htm," "beg_meetings.htm," "beg_links.htm," and "beg_help.htm."

beg_members.htm:

The members page, now found at beg_members.htm, has a new look. Check it out (and let me know of any errors). As usual, the individual members' entries can be reached from the members list on the BEG splash page.

sta0010.htm is (almost) no more:

The members' publications page is now found at bib_members.htm and has a new look. Please check it out, using this page especially to make sure that the BEG bibliography entry of *your* publications do not contain errors and that their abstract (if it exists) is present and correct!!!

phage companies:

This, I hope, will become the definitive list of phage companies. Mainly these are phage-therapy companies, though I am willing to list anything that is attempting to (legally) make money off of the application of bacteriophages. Currently five (six?) companies are listed. Please

keep sending those names in.

beg_join.htm:

This page is a new home for instructions to potential members, formerly found only on the pages of *BEG News* in the New Members section. There is now a link to this page from the BEG splash page.

beg.htm:

The Bacteriophage Ecology Group now has a site map/index. Check it out.

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Upcoming Meetings

The BEG Meetings link will continue, but reminders about upcoming meetings will be placed in this section of *BEG News*. If you know of any meetings that might be of interest to BEG members, please send this information for posting to abedon.1@osu.edu or to "BEG Meetings," *Bacteriophage Ecology Group News*, care of Stephen T. Abedon, Department of Microbiology, The Ohio State University, 1680 University Dr., Mansfield, Ohio 44906.

Evergreen International Phage Meeting:

The above web link still refers to 1998's meeting. This year's meeting will be held in Montreal, *not* Olympia, Washington, from June 7 to June 11, 2000. The meeting will cover all aspects of phage biology, from basic mechanisms and molecular biology to phage ecology and phage therapy. The 1998 meeting had a strong bacteriophage ecology presence and with luck (i.e., with your participation!) we will do even better in 2000. Stay tuned for information on how to register on line.

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Jobs

The BEG Employment / Job Listings page will no longer be maintained. Instead, any job listings will be found in this section of *BEG News*. If you are looking to*fill* a bacteriophage-ecology related position or are in *search of* a bacteriophage-ecology related position, please feel free to advertise as s uch here (there will be no charge, of course). Legitimate information only, please, and *BEG News* cannot be held responsible for any incorrect information supplied by posters. Send any information for posting to abedon.1@osu.edu or to "BEG Jobs," *Bacteriophage Ecology Group News*, care of Stephen T. Abedon, Department of Microbiology, The Ohio State University, 1680 University Dr., Mansfield, Ohio 44906.

No entry.

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Submissions

Submissions are non-editorial items describing or highlighting some aspect of bacteriophage ecology including news pieces, historical pieces, reviews, and write- ups of research. Peer review of submissions is possible and a desire for peer review should be indicated. Send all submissions to abedon.1@osu.edu or to "Submissions", Bacteriophage Ecology Group News, care of Stephen T. Abedon, Department of Microbiology, The Ohio State University, 1680 University Dr., Mansfield, Ohio 44906. Please send all submissions as Microsoft Word documents, if possible (I'll let you know if I have trouble converting any other doc ument formats), and in English.

Obituary: Hansjürgen Raettig - Collector of Bacteriophage References

(October 12, 1911 - December 1, 1997)

Hansjürgen Raettig, MD, was born in Stralsund, Germany. He studied medicine and obtained his medical degree in 1939. His doctoral thesis was on the influence of season and climate on pulmonary embolies. His early career can be summarized as follows. He was induced into the army in 1939, worked during the war in a military hospital in France and in the Hygiene Institute in Greifswald, was a member of the Public Health Institute of the same city from 1946 to 1948, and was recruited in 1948 by the Robert-Koch-Institute in Berlin. The institute was then in dire straights, lacking basic furnitures and facilities, yet charged with heavy public health responsibilities. In 1952 Dr. Raettig became the equivalent of an assistant professor at the Free University of Berlin. He became a full professor in 1961 and then became acting director of the Robert-Koch-Institute, holding that position from July 10 of that year until March 7, 1976 and retiring from the institute October 10, 1976.

Dr. Raettig published more than 200 papers or books. Most were on vaccination, namely against typhoid fever, shigellosis, poliomyelitis, and cholera. He was also very concerned with epidemiology, public health, and seriological diagnosis of infectious diseases. In the early fifties, he became interested in bacteriophages, mainly in intestinal phages and their variability. This led to experimentation with phage media and inactivation experiments and culminated in a two-volume book entitled "*Bakteriophagie*", a literature documentation aimed at covering the whole vast phage literature and classifying it by using a large number of key-words. Two volumes covered the literature from 1915 to 1956 and from 1956 to 1965, respectively. The first volume was in German only and the second one was in English and German [Raettig, H., 1958, *Bakteriophagie, 1917 bis 1956; Zugleich en Vorschlag zur Dokumentation Wissenschaftlicher Literatur* & 1967, *Bakteriophagie 1957-1965* (*Bacteriophagy 1957-1965*), both G. Fischer, Stuttgart]. The two

volumes covered a total of 11,405.

Dr. Raettig was also interested in electron microscopy and offered a course on this subject which I had the good fortune to attend in 1958 or 1959. I remember him as a friendly and engaging teacher who took great pried to show how he had assembled and categorized the vast phage literature using perforated cards. The book "*Bakteriophagie*" is now a bibliophile rarity, much sought after by phage workers and extremely useful for its near complete coverage of the early literature on this subject. To my knowledge, nobody in the field of biology has ever assembled a similarly vast and structured documentation. It is certainly Dr. Raettig's most enduring legacy.

Hans-Wolfgang Ackermann
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ackermann@mcb.ulaval.ca

Submission Archive

- On an Invisible Microbe Antagonistic to the Dysentery Bacillus by Felix d'Herelle
- Obituary: Hansjürgen Raettig - Collector of Bacteriophage References (October 12, 1911 - December 1, 1997)

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Letters

Letters should consist of comments, short statements, or personal editorials. Send all letters to abedon.1@osu.edu or to "Letters", Bacteriophage Ecology Group News, care of Stephen T. Abedon, Department of Microbiology, The Ohio State University, 1680 University Dr., Mansf ield, Ohio 44906. Please send all letters in English and all mailed or attached letters as Microsoft Word documents, if possible (I'll let you know if I have trouble converting any other document formats). In addition, to standard letters, BEG receives questions on a regular basis that may be addressed by BEG members. These qu estions are listed below. Anybody interested in answering these questions through *BEG News*, e-mail me at the following address: abedon.1@osu.edu. Alternatively, answer through the prompt following each question. Please note that these questions have n ot been edited for grammar, spelling, or clarity.

No entry.

Questions

No entry.

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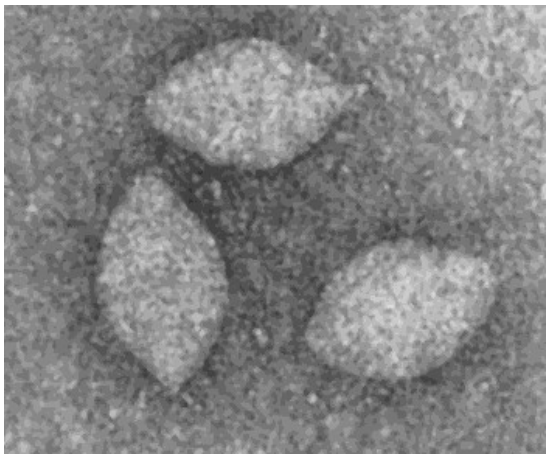
Phage Images

Please send any phage images that you would like to present in this section to "Phage Images," *The Bacteriophage Ecology Group*, care of Stephen T. Abedon, Department of Microbiology, The Ohio State University, 1680 University Dr., Mansfield, Ohio 44906. Alternatively, you may scan the images yourself and send them as an attachment to abedon.1@osu.edu. Please save all scans in gif or jpg formats and preferably with an image size (in terms of width, height, and kbytes) that will readily fit on a standard web page.



Phage Image Archive

- The Face of the Phage
- Bacteriophage T2 by H.-W. Ackermann
- SSV1-Type Phage

New Publications

New bacteriophage publications are listed below. Each quarter not-yet-listed publications from the previous two years will be presented along with their abstracts. The indicator "???" denotes, of course, that specific information is not yet in the BEG Bibliography. Please help in the compilation of the BEG Bibliography by supplying any updated information, correcting any mistakes, and, of course, sending the references to your bacteriophage ecology publications, as well as the references to any bacteriophage ecology publications that you know of but which are not yet in the bibliography (send to abedon.1@osu.edu or to "BEG Bibliography," *Bacteriophage Ecology Group News*, care of Stephen T. Abedon, Department of Microbiology, The Ohio State University, 1680 University Dr., Mansfield, Ohio 44906). Also, be sure to indicate any listed publications that you feel should not be presented in the BEG Bibliography. This list is also present with available abstracts at the end of *BEG News*.

1. Viruses help fight bacteria that resist antibiotics. ??? (1999). *The Patriot Ledger Quincy, MA* 13:183? (News Section)-same? [PRESS FOR ABSTRACT]

2. Bacteriophage T4 resistance to lysis-inhibition collapse. Abedon, S. T. (1999). *Genetical Research* 74:1-11. [PRESS FOR ABSTRACT]

3. Tailed bacteriophages: the order caudovirales. Ackermann, H.-W. (1998). *Advances in Virus Research* 51:135-201. [PRESS FOR ABSTRACT]

4. Vyiavlenie roli divergentsii v evoliutsii fagov-transpozonov gruppy B3 *Pseudomonas aeruginosa* [Role of divergence in evolution of group B3 *Pseudomonas aeruginosa* transposable phage evolution]. Akhverdian, V. Z., Khrenova, E. A., Lobanov, A. O., Krylov, V. N. (1998). *Genetika* 34:846-849. [PRESS FOR ABSTRACT]

5. Rekominatsionnoe proiskhozhdenie prirodnykh fagov-transpozonov rodstvennykh vidov gruppy B3, aktivnykh na bakteriiakh vida *Pseudomonas aeruginosa* [Recombinational origin of natural transposable phages of related species belonging to group B3, active in *Pseudomonas aeruginosa* species]. Akhverdian, V. Z., Lobanov, A. O., Khrenova, E. A., Krylov, V. N. (1998). *Genetika* 34:697-700. [PRESS FOR ABSTRACT]

6. Ispol'zovanie adaptirovannogo sal'monelleznogo bakteriofaga v praktike lecheniia i profilaktiki nozokomial'nogo sal'monelleza [Practical use of adapted *Salmonella* bacteriophage for the treatment and prevention of nosocomial infections]. Akimkin, V. G., Bondarenko, V. M., Voroshilova, N. N., Darbeeva, O. S., Baiguzina, F. A. (1998). *Zhurnal Mikrobiologii, Epidemiologii i Immunobiologii* 85-86. [PRESS FOR ABSTRACT]

7. Phage-encoded genes and *Salmonella* virulence. Ali, T. R., Pallen, M. J. (1998). *Molecular Microbiology* 28:1039-1041. [PRESS FOR ABSTRACT]

8. Virus removal from bioproducts using ultrafiltration membranes modified with latex particle pretreatment. Bellara, S. R., Cui, Z., MacDonald, S. L., Pepper, D. S. (1998). *Bioseparation* 7:79-88. [PRESS FOR ABSTRACT]

9. Viral evolution revealed by bacteriophage PRD1 and human adenovirus coat protein structures. Benson, S. D., Bamford, J. K., Bamford, D. H., Burnett, R. M. (1999). *Cell* 98:825-833. [PRESS FOR ABSTRACT]

10. Isolation of *Shigella sonnei* lysogenic for a bacteriophage encoding gene for production of Shiga toxin. Beutin, L., Strauch, E., Fischer, I. (1999). *Lancet* 353:1498-1498. [no abstract]

11. Two high-frequency-transduction phage isolates from lysogenic strains of *Pseudomonas aeruginosa* transducing antibiotic resistance. Blahova, J., Kralikova, K., Krcmery, V. Sr., Mikovicova, A., Bartonicova, N. (1998). *Acta Virologica* 42:175-179. [PRESS FOR ABSTRACT]

12. Antimicrobial properties and morphological characteristics of two *Photorhabdus luminescens* strains. Bondi, M., Messi, P., Sabia, C., Baccarani Contri, M., Manicardi, G. (1999). *New Microbiologica* 22:117-127. [PRESS FOR ABSTRACT]

13. A natural longer glycine-rich region in IKe filamentous phage confers no selective advantage. Bruno, R., Bradbury, A. (1998). *Gene* 184:121-123. [PRESS FOR ABSTRACT]

14. Search for bacteriophages spontaneously occurring in cultures of haemolytic intestinal spirochaetes of human and animal origin. Calderaro, A., Dettori, G., Grillo, R., Plaisant, P., Amalfitano, G., Chezzi, C. (1998). *Journal of Basic Microbiology* 38:313-322. [PRESS FOR ABSTRACT]

15. Bacteriophages induced from weakly beta-haemolytic human intestinal spirochaetes by mitomycin C. Calderaro, A., Dettori, G., Collini, L., Ragni, P., Grillo, R., Cattani, P., Fadda, G., Chezzi, C. (1998). *Journal of Basic Microbiology* 38:323-335. [PRESS FOR ABSTRACT]

16. Lysogenic bacteriophage M1 from *Selenomonas ruminantium*: isolation, characterization and DNA sequence analysis of the integration site. Cheong, J. P., Brooker, J. D. (1998). *Microbiology* 144:2195-2202. [PRESS FOR ABSTRACT]

17. Genetic organization and functional analysis of a novel phage abortive infection system, AbiL, from *Lactococcus lactis*. Deng, Y. M., Liu, C. Q., Dunn, N. W. (1999). *Journal of Biotechnology* 67:135-149. [PRESS FOR ABSTRACT]

18. Survival, physiology, and lysis of *Lactococcus lactis* in the digestive tract. Drouault, S. (1999). *Applied and Environmental Microbiology* 65:4881-4886. [PRESS FOR ABSTRACT]

19. Integrity of powder-free examination gloves to bacteriophage penetration. Edlich, R. F. (1999). *J. Biomed. Mater. Res.* 48:755-758. [PRESS FOR ABSTRACT]

20. Evaluation of reverse transcription-PCR and a bacteriophage-based assay for rapid phenotypic detection of rifampin resistance in clinical isolates of *Mycobacterium tuberculosis*. Eltringham, I. J. (1999). *J. Clin. Microbiol.* 37:3524-3527. [PRESS FOR ABSTRACT]

21. Evaluation of a bacteriophage-based assay (Phage amplified biologically assay) as a rapid screen for resistance to isoniazid, ethambutol, streptomycin, pyrazinamide, and ciprofloxacin among clinical isolates of *Mycobacterium tuberculosis*. Eltringham, I. J. (1999). *J. Clin. Microbiol.* 37:3528-3532. [PRESS

FOR ABSTRACT]

22. rexB of bacteriophage lambda is an anti-cell death gene. Engelberg-Kulka, H., Reches, M., Narasimhan, S., Schoulaker-Shwarz, R., Klemes, Y., Aizenman, E., Glaser, G. (1998). *Proceedings of the National Academy of Sciences, USA* 95:15481-15486. [PRESS FOR ABSTRACT]

23. Epidemiology, genetics, and ecology of toxigenic *Vibrio cholerae*. Faruque, S. M., Albert, M. J., Mekalanos, J. J. (1998). *Microbiology and Molecular Biology Reviews* 62:1301-314. [PRESS FOR ABSTRACT]

24. Assessment of the effects of various UV sources on inactivation and photoproduct induction in phage T7 dosimeter. Fekete, A., Vink, A. A., Gaspar, S., Berces, A., Modos, K., Ronto, G., Roza, L. (1998). *PHOTOCHEMISTRY AND PHOTOBIOLOGY* 68:527-531. [PRESS FOR ABSTRACT]

25. Inducible prophages contribute to *Salmonella* virulence in mice. Figueroa-Bossi, N., Bossi, L. (1999). *Molecular Microbiology* 33:167-176. [PRESS FOR ABSTRACT]

26. Genome structure of mycobacteriophage D29: implications for phage evolution. Ford, M. E., Sarkis, G. J., Belanger, A. E., Hendrix, R. W., Hatfull, G. F. (1998). *Journal of Molecular Biology* 279:143-164. [PRESS FOR ABSTRACT]

27. Identification of four phage resistance plasmids from *Lactococcus lactis* subsp. cremoris HO2. Forde, A., Daly, C., Fitzgerald, G. F. (1999). *Applied and Environmental Microbiology* 65:1540-1547. [PRESS FOR ABSTRACT]

28. Bacteriophage defence systems in lactic acid bacteria. Forde, A. (1999). *Antonie van Leeuwenhoek* 76:89-113. [PRESS FOR ABSTRACT]

29. Sravnitel'noe izuchenie bakteriofagov *Morganella* i *Providencia* [Comparative study of *Morganella* and *Providencia* bacteriophages]. Gabrilovich, I. M., Zarochensev, M. V., Saimov, S. R. (1998). *Zhurnal Mikrobiologii, Epidemiologii i Immunobiologii* 5:20-22. [PRESS FOR ABSTRACT]

30. Phage restriction and the presence of small plasmids in *Salmonella enteritidis*. Gado, I., Laszlo, V. G., Nagy, B., Milch, H., Drin, I., Awad-Masalmeh, M., Horvath, J. (1998). *Zentralblatt Fur Bakteriologie* 287:509-519. [PRESS FOR ABSTRACT]

31. A species barrier between bacteriophages T2 and T4: exclusion, join-copy and join-cut-copy recombination and mutagenesis in the dCTPase genes. Gary, T. P., Colowick, N. E., Mosig, G. (1998). *Genetics* 148:1461-1473. [PRESS FOR ABSTRACT]

32. Roles of *Pseudomonas aeruginosa* las and rhl quorum-sensing systems in control of twitching motility. Glessner, A., Smith, R. S., Iglewski, B. H., Robinson, J. B. (1999). *Journal of Bacteriology* 181:1623-1629. [PRESS FOR ABSTRACT]

33. Metastabil'nost' fenotipa u bakterii [Metastable phenotype of bacteria]. Golovlev, E. L. (1998). *Mikrobiologica* 67:149-155. [PRESS FOR ABSTRACT]

34. The use of a fluorescent bacteriophage assay for detection of *Escherichia coli* O157:H7 in inoculated ground beef and raw milk. Goodridge, L., Chen, J., Griffiths, M. (1999). *International Journal of Food Microbiology* 47:43-50. [PRESS FOR ABSTRACT]

35. Development and characterization of a fluorescent-bacteriophage assay for detection of *Escherichia coli* O157:H7. Goodridge, L., Chen, J., Griffiths, M. (1999). *Applied and Environmental Microbiology* 65:1397-1404. [PRESS FOR ABSTRACT]

36. Bacteriophage and associated polysaccharide depolymerases--novel tools for study of bacterial biofilms [published erratum appears in J Appl Microbiol 1999 Feb;86(2):359]. Hughes, K. A., Sutherland, I. W., Clark, J., Jones, M. V. (1998). *Journal of Applied Microbiology* 85:583-590. [PRESS FOR ABSTRACT]

37. Targeted delivery of multivalent phage display vectors into mammalian cells. Ivanenkov, V., Felici, F., Menon, A. G. (1998). *Biochimica et Biophysica Acta* 1448:463-472. [PRESS FOR ABSTRACT]

38. Uptake and intracellular fate of phage display vectors in mammalian cells. Ivanenkov, V., Felici, F., Menon, A. G. (1998). *Biochimica et Biophysica Acta* 1448:450-462. [PRESS FOR ABSTRACT]

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41. The hunt is on for new ways to overcome bacterial resistance. Knudson, M. (1998). *Technology Review* 100:22-30? [PRESS FOR ABSTRACT]

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59. Inactivation of *Lactobacillus helveticus* bacteriophages by thermal and chemical treatments. Quiberoni, A. (1999). *J. Food. Prot.* 62:894-898. [PRESS FOR ABSTRACT]

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63. Characterisation of 16 *Campylobacter jejuni* and *C. coli* typing bacteriophages. Sails, A. D., Wareing, D. R., Bolton, F. J., Fox, A. J., Curry, A. (1998). *Journal of Medical Microbiology* 47:123-128. [PRESS FOR ABSTRACT]

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66. *Pseudomonas aeruginosa* phage lysate as an immunobiological agent. 1. Selection of *Pseudomonas aeruginosa* clinical strains for phage lysate preparation. Sekaninova, G., Kolarova, M., Pillich, J., Semenka, J., Slavikova, H., Kubickova, D., Zajicova, V. (1999). *Folia Microbiologica* 44:93-97. [PRESS FOR ABSTRACT]

67. Sunlight inactivation of fecal bacteriophages and bacteria in sewage-polluted seawater. Sinton, L. W., Finlay, R. K., Lynch, P. A. (1999). *Applied and Environmental Microbiology* 65:3605-3613. [PRESS FOR ABSTRACT]

68. Images in Infectious Diseases in Obstetrics and Gynecology. Vaginal *Lactobacillus* phage plaques and electron micrograph. Tao, L., Pavlova, S. I. (1999). *Infectious Diseases in Obstetrics and Gynecology* 6:236-236. [no abstract]

69. Genome plasticity in the distal tail fiber locus of the T-even bacteriophage: recombination between conserved motifs swaps adhesin specificity. Tetart, F., Desplats, C., Krisch, H. M. (1998). *Journal of Molecular Biology* 282:543-556. [PRESS FOR ABSTRACT]

70. Modeling the oddities of biology. Trivedi, B. (1998). *Nature Biotechnology* 16:1316-1317. [no abstract]

71. The clinically isolated FIZ15 bacteriophage causes lysogenic conversion in *Pseudomonas aeruginosa* PAO1. Vaca-Pacheco, S., Paniagua-Contreras, G. L., Garcia-Gonzalez, O., de la Garza, M. (1999). *Current Microbiology* 38:239-243. [PRESS FOR ABSTRACT]

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262:104-113. [PRESS FOR ABSTRACT]

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74. Bacteriophage diversity in the North Sea. Wichels, A., Biel, S. S., Gelderblom, H. R., Brinkhoff, T., Muyzer, G., Schutt, C. (1998). *Applied and Environmental Microbiology* 64:4128-4133. [PRESS FOR ABSTRACT]

75. Biodistribution of filamentous phage-Fab in nude mice. Yip, Y. L., Hawkins, N. J., Smith, G., Ward, R. L. (1999). *Journal of Immunological Methods* 226:171-178. [PRESS FOR ABSTRACT]

76. Amplification and spread of viruses in a growing plaque. You, L. (1999). *Journal of Theoretical Biology* 200:365-373. [PRESS FOR ABSTRACT]

77. Svoistva mikobakteriofaga MTPN11 [Properties of MTPN11 mycobacteriophage]. Zhilenkov, E. L., Shemakin, I. G., Stepanshina, V. N., Korobova, O. V., Oborotov, M. V., Dorozhkova, I. R. (1998). *Mikrobiologica* 67:660-665. [PRESS FOR ABSTRACT]

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New Publications with Abstracts

For your convenience, a list of new publications without associated abstracts (but with links to abstracts) is found above. The list presented below is identical to the above list except that abstracts are included.

1. **Viruses help fight bacteria that resist antibiotics. ??? (1999). *The Patriot Ledger Quincy, MA* 13:183? (News Section)-same?** Scientists have harnessed nature's way of tackling antibiotic- resistant bacteria. An injection of a virus that attacks bacteria only has saved the life of a patient after all other drugs proved useless. The technique -- the use of bacteriophages, or bacteria-eaters -- was pioneered in the former Soviet Union at around the time of the discovery of much more swiftly effective antibiotics. Although penicillin and other such drugs changed medicine, one team in Tbilisi, Georgia, kept research in phages going to the present day.

2. **Bacteriophage T4 resistance to lysis-inhibition collapse. Abedon, S. T. (1999). *Genetical Research* 74:1-11.** Lysis-inhibition is a mechanism of latent-period extension and burst-size increase that is induced by the T4 bacteriophage adsorption of T4-infected cells. Mutants of T4 genes *imm*, *sp*, and *5* (specifically the *ts1* mutant of the latter) display some lysis inhibition. However, these mutants experience lysis-inhibition collapse, the lysis of lysis-inhibited cells, earlier than wild type-infected cells (i.e., their collapse occurs *prematurely*). Lysis from without is a lysis induced by excessive T4 adsorption. Gp*5* is an inducer of lysis from without while gp*imm* and gp*sp* effect resistance to lysis from without. This paper shows that interfering with the adsorption of phages to *imm*-, *sp*-, or *5ts*1-mutant-infected cells, in a variety of contexts, inhibits premature lysis-inhibition collapse. From these data, it is inferred that wild-type T4-infected cells display resistance to lysis-inhibition collapse by a mechanism resembling resistance to lysis from without.

3. **Tailed bacteriophages: the order caudovirales. Ackermann, H.-W. (1998). *Advances in Virus Research* 51:135-201.** Tailed bacteriophages have a common origin and constitute an order with three families, named Caudovirales. Their structured tail is unique. Tailed phages share a series of high-level taxonomic properties and show many facultative features that are unique or rare in viruses, for example, tail appendages and unusual bases. They share with other viruses, especially herpesviruses, elements of morphogenesis and life-style that are attributed to convergent evolution. Tailed phages present three types of lysogeny, exemplified by phages lambda, Mu, and P1. Lysogeny appears as a secondary property acquired by horizontal gene transfer. Amino acid sequence alignments (notably of DNA polymerases, integrases, and peptidoglycan hydrolases) indicate frequent events of horizontal gene transfer in tailed phages. Common capsid and tail proteins have not been detected. Tailed phages possibly evolved from small protein shells with a few genes sufficient for some basal level of productive infection. This early stage can no longer be traced. At one point, this precursor phage became perfected. Some of its features were perfect enough to be transmitted until today. It is tempting to list major present-day properties of tailed phages in the past tense to construct a tentative history of these viruses: 1. Tailed phages originated in the early Precambrian, long before eukaryotes and their viruses. 2. The ur-tailed phage, already a quite evolved virus, had an icosahedral head of about 60 nm in diameter and a long non-contractile tail with sixfold symmetry. The capsid contained a single molecule of dsDNA of about 50 kb, and the tail was probably provided with a fixation apparatus. Head and tail were held together by a connector. a. The particle contained no lipids, was heavier than most viruses to come, and had a high DNA content proportional to its capsid size (about 50%). b. Most of its DNA coded for structural proteins. Morphopoietic genes clustered at one end of the genome, with head genes preceding tail genes. Lytic enzymes were probably coded for. A part of the phage genome was nonessential and possibly bacterial. Were tailed phages general transductants since the beginning? 3. The virus infected its host from the outside, injecting its DNA. Replication involved transcription in several waves and formation of DNA concatemers. Novel phages were released by burst of the infected cell after lysis of host membranes by a peptidoglycan hydrolase (and a holin?). a. Capsids were assembled from a starting point, the connector, and around a scaffold. They underwent an elaborate maturation process involving protein cleavage and capsid expansion. Heads and tails were assembled separately and joined later. b. The DNA was cut to size and entered preformed capsids by a headful mechanism. 4. Subsequently, tailed phages diversified by: a. Evolving contractile or short tails and elongated heads. b. Exchanging genes or gene fragments with other phages. c. Becoming temperate by acquiring an integrase-excisionase complex, plasmid parts, or transposons. d. Acquiring DNA and RNA polymerases and other replication enzymes. e. Exchanging lysin genes with their hosts. f. Losing the ability to form concatemers as a consequence of acquiring transposons (Mu) or proteinprimed DNA polymerases (phi 29). Present-day tailed phages appear as chimeras, but their monophyletic origin is still inscribed in their morphology, genome structure, and replication strategy. It may also be evident in the three-dimensional structure of capsid and tail proteins. It is unlikely to be found in amino acid sequences because constitutive proteins must be so old that relationships were obliterated and most or all replication-, lysogeny-, and lysis-related proteins appear to have been borrowed. However, the sum of tailed phage properties and behavior is so characteristic that tailed phages cannot be confused with other viruses.

4. **Vyiavlenie roli divergentsii v evoliutsii fagov-transpozonov gruppy B3 *Pseudomonas aeruginosa* [Role of divergence in evolution of group B3 *Pseudomonas aeruginosa* transposable phage evolution]. Akhverdian, V. Z., Khrenova, E. A., Lobanov, A. O., Krylov, V. N. (1998). *Genetika* 34:846-849.** A heteroduplex analysis was performed to identify and map divergent DNA sequences in the genomes of the P. aeruginosa transposable phages (TPs) of group B3 using different formamide concentrations (30, 50, and 70%). Six PTs were classified into three related species--B3, PM681, and PM57. The role of DNA divergence in the evolution of TPs within one species is insignificant: the genomes of phages pM105 and PM681 (species PM681) and phages Hw12 and pM57 (species pM57) were shown to contain either homologous (98%) or nonhomologous DNA (2%). Homologous, divergent, and nonhomologous DNA regions (modules) were identified in the genomes of the TP of different species. Homologous modules with a level of DNA homology higher than 86% constitute approximately 30% of the phage genome; they are located at the left (1-5 kb) and right (29-38 kb) ends of the phage genome. Divergent modules with a DNA homology level between 50 and 67% and nonhomologous modules represent 30 to 35% and 25 to 30% of the phage genome, respectively. These regions form a mosaic structure in a 5-29-kb region. Thus, the key role of DNA divergence in the evolution of the natural TPs of three

related species of group B3 was shown. A single region containing a 5-11-kb divergent DNA sequence was detected in the pM62 phage genome (species pM57). As shown by our previous data, this region was integrated into phage pM62 via interspecific recombination with a phage of species B3.

5. **Rekominatsionnoe proiskhozhdenie prirodnykh fagov-transpozonov rodstvennykh vidov gruppy B3, aktivnykh na bakteriiakh vida *Pseudomonas aeruginosa* [Recombinational origin of natural transposable phages of related species belonging to group B3, active in *Pseudomonas aeruginosa* species]. Akhverdian, V. Z., Lobanov, A. O., Khrenova, E. A., Krylov, V. N. (1998). *Genetika* 34:697-700.** A heteroduplex analysis of four related transposable phages--B3, PM57, PM62, and Hw12--of the Pseudomonas aeruginosa B3 group was performed. Heteroduplex structures, restriction maps, and data on DNA-DNA hybridization obtained upon hybridization of phage DNA restriction fragments with labeled probes representing different regions of the phage genomes are in good agreement. The data obtained strongly confirmed the recombinational origin of the analyzed phages. Thus, all natural transposable phages of P. aeruginosa, including phages from both group B3 and species D3112, were shown to have a recombinational origin.

6. **Ispol'zovanie adaptirovannogo sal'monelleznogo bakteriofaga v praktike lecheniia i profilaktiki nozokomial'nogo sal'monelleza [Practical use of adapted *Salmonella* bacteriophage for the treatment and prevention of nosocomial infections]. Akimkin, V. G., Bondarenko, V. M., Voroshilova, N. N., Darbeeva, O. S., Baiguzina, F. A. (1998). *Zhurnal Mikrobiologii, Epidemiologii i Immunobiologii* 85-86.**

7. **Phage-encoded genes and *Salmonella* virulence. Ali, T. R., Pallen, M. J. (1998). *Molecular Microbiology* 28:1039-1041.**

8. **Virus removal from bioproducts using ultrafiltration membranes modified with latex particle pretreatment. Bellara, S. R., Cui, Z., MacDonald, S. L., Pepper, D. S. (1998). *Bioseparation* 7:79-88.** Ultrafiltration is an attractive process for virus removal from bioproducts owing to its high throughput as well as the fact that the operation is carried out under ambient conditions (damage to proteins is highly limited). The principal concern regarding the adoption of conventional ultrafiltration membranes for virus removal is the possibility of the virus passing through abnormally large pores or surface imperfections on the membrane surface. The chief principle behind the present work is to pretreat the membrane by blocking the abnormally large pores using latex particles. Experimental work was conducted to validate this pretreatment using the bacteriophage phi x 174 as a model virus. The results attained were highly encouraging. Different sizes of latex particles were tested by treating a 100 KD molecular weight cut-off membrane, and the transmission of phage (suspended in buffer) through this membrane assessed. In the absence of any particle pretreatment, a virus clearance of 4.78 log reduction value was observed for this membrane. The transmission of phage through the membrane could be reduced by an order of magnitude using 0.11 micron latex particles, or two orders of magnitude using a combination of 0.11 and 0.50 micron particles. The application of latex particles did not hinder the transport of protein through the 100 KD membrane. Protein sieving coefficients obtained using this membrane were 91%, 16% and 2%, for lysozyme, HSA and IgG, respectively.

9. **Viral evolution revealed by bacteriophage PRD1 and human adenovirus coat protein structures. Benson, S. D., Bamford, J. K., Bamford, D. H., Burnett, R. M. (1999). *Cell* 98:825-833.** The unusual bacteriophage PRD1 features a membrane beneath its icosahedral protein coat. The crystal structure of the major coat protein, P3, at 1.85 A resolution reveals a molecule with three interlocking subunits, each with two eight-stranded viral jelly rolls normal to the viral capsid, and putative membrane-interacting regions. Surprisingly, the P3 molecule closely resembles hexon, the equivalent protein in human adenovirus. Both viruses also have similar overall architecture, with identical capsid lattices and attachment proteins at their vertices. Although these two dsDNA viruses infect hosts from very different kingdoms, their striking similarities, from major coat protein through capsid architecture, strongly suggest their evolutionary relationship.

10. **Isolation of *Shigella sonnei* lysogenic for a bacteriophage encoding gene for production of Shiga toxin. Beutin, L., Strauch, E., Fischer, I. (1999). *Lancet* 353:1498-1498.**

11. **Two high-frequency-transduction phage isolates from lysogenic strains of *Pseudomonas aeruginosa* transducing antibiotic resistance. Blahova, J., Kralikova, K., Krcmery, V. Sr., Mikovicova, A., Bartonicova, N. (1998). *Acta Virologica* 42:175-179.** Two high frequency transduction (HFT) phage isolates, obtained from seriously ill patients, transducing individual determinants of antibiotic resistance with a frequency of 10(-5) (phage isolate AP-103) and 10 (-6) (phage isolate AP-343), are described. The frequency of transduction depended on the transduced determinant(s) of resistance used for the detection of transductants and on the individual recipient antibiotic-susceptible strain of Pseudomonas aeruginosa (PAO and/or ML series). A multiple-antibiotic resistance was transduced by the phage isolate AP-343 to all tested recipient strains. The appearance of such phages in clinical conditions with an unusually high frequency of transduction might contribute to the dissemination of antibiotic resistance genes among nosocomial strains of P. aeruginosa. The existence of HFT phages might reflect an increased efficiency of transduction of antibiotic resistance among P. aeruginosa strains, and thus an increased risk of spread of antibiotic resistance even to recently introduced anti-pseudomonadal antibiotics among pseudomonads with unfavourable and unwanted epidemiological consequences in hospital conditions.

12. **Antimicrobial properties and morphological characteristics of two *Photorhabdus luminescens* strains. Bondi, M., Messi, P., Sabia, C., Baccarani Contri, M., Manicardi, G. (1999). *New Microbiologica* 22:117-127.** The biological properties of two Photorhabdus luminescens isolates (MU1 and MU2) of environmental source and the activity of antimicrobial agar diffusible agents (AADA) produced by the same are reported. With regard to cultural features, two variant forms for P. luminescens MU1 and three for P. luminescens MU2 (including an intermediate phase I-like form) have been found. These three forms differ in biological and biochemical properties: beta-lactamase, urease, bioluminescence and antimicrobial agar diffusible substance production associated with the phase I form, were less evident in the intermediate phase I-like MU2 and were absent in phase II form. Antimicrobial activity was present in both strains, with the production of a large amount of a diffusible compound with a wide spectrum of action against bacteria of other genera; a reduced activity against correlated species was also observed. Examination by electron microscopy of MU1 and MU2 purified broth cultures revealed the presence of particles belonging to the class of the phage tail-like bacteriocins, described in recent studies as responsible for antibacterial activity against correlated bacteria, a result never confirmed "in vitro". A plasmid of 21 Mdal was observed in all the form variants of P. luminescens MU2, suggesting that plasmids are not involved in the transition from primary to secondary phase; no plasmid was detected in P. luminescens MU1.

13. **A natural longer glycine-rich region in IKe filamentous phage confers no selective advantage. Bruno, R., Bradbury, A. (1998). *Gene* 184:121-123.** Filamentous phage infect bacteria bearing pili. The phage protein involved in the recognition of pili and subsequent penetration of the phage into bacteria is the gene 3 protein (g3p). This is a multi-domain protein with glycine-rich regions separating some of the domains. Here we have found an insertion within the glycine-rich domain of the g3p of IKe, a filamentous phage which infects bacteria bearing N pili. Although this insertion considerably increases the length of the glycine-rich domain it has no selective advantage or disadvantage in infection or production of phage, and can therefore be considered a neutral mutation.

14. **Search for bacteriophages spontaneously occurring in cultures of haemolytic intestinal spirochaetes of human and animal origin. Calderaro, A., Dettori, G., Grillo, R., Plaisant, P., Amalfitano, G., Chezzi, C. (1998). *Journal of Basic Microbiology* 38:313-322.** An electron microscopic survey of the occurrence of bacteriophages which appear spontaneously in cultures of haemolytic intestinal spirochaetes of human and animal origin was made. Excluding one isometric tailed phage particle which was observed in the form of free particle in proximity to a spirochaete of the w beta HIS strain HRM18, bacteriophages were never observed while examining cells of 21 weakly beta-haemolytic human intestinal spirochaetes (w beta HIS), swine Serpulina pilosicoli strain P43/6/78, and the avian strain 1380, although 50-100 cells of each spirochaetal strain were analysed. Isometric tailed bacteriophages were found associated with only three out of the 100 cells of strongly beta-haemolytic swine Serpulina hyodysenteriae strain P18A comparatively analysed. According to our results and previous published reports, the occurrence of bacteriophages which appear spontaneously in cultures of intestinal spirochaetes is a rare event.

15. **Bacteriophages induced from weakly beta-haemolytic human intestinal spirochaetes by mitomycin C. Calderaro, A., Dettori, G., Collini, L., Ragni, P., Grillo, R., Cattani, P., Fadda, G., Chezzi, C. (1998). *Journal of Basic Microbiology* 38:323-335.** A comparative electron microscopic analysis of weakly beta-haemolytic spirochaetes related to human and animal intestinal spirochaetosis was done in order to search for the presence of inducible bacteriophages associated with these spirochaetes. Bacteriophages were detected at the electron microscope after experimental induction with mitomycin C in 4 strains of weakly beta-haemolytic spirochaetes related to human intestinal spirochaetosis, in Serpulina pilosicoli strain P43/6/78, the causative agent of swine intestinal spirochaetosis, in a spirochaetal strain related to avian intestinal spirochaetosis, and in Serpulina hyodysenteriae, strain P18A, the causative agent of swine dysentery, which was comparatively analysed as control. All phage-particles observed in both human and animal intestinal spirochaetes were morphologically similar with an isometric head of 45 nm diameter and a tail 63-70 nm long and 7-12 nm width. The presence of morphologically similar phages in all the haemolytic intestinal spirochaetes of human and animal origin analysed in this study opens some important questions, about the genetic relationship of phages present in pathogenic intestinal spirochaetes, their host range, and the possibility of natural gene transfer among pathogenic haemolytic intestinal spirochaetes of human and animal origin.

16. **Lysogenic bacteriophage M1 from *Selenomonas ruminantium*: isolation, characterization and DNA sequence analysis of the integration site. Cheong, J. P., Brooker, J. D. (1998). *Microbiology* 144:2195-2202.** Bacteriophage M1 from the ruminal bacterium Selenomonas ruminantium strain ML12 comprises a 30 nm icosahedral capsid, a 25 nm tail and 48 kb of linear dsDNA with cohesive ends. A restriction map of the phage genome has been constructed. The presence of bacteriophage M1 in the rumen has been demonstrated by PCR amplification and Southern blot analysis of DNA from rumen bacterial samples obtained from ten different sheep. Lysogeny was demonstrated by hybridization of M1 DNA to host chromosomal DNA and by identification and cloning of a 2.3 kb region of the phage containing the predicted attP domain which promotes chromosomal integration. DNA sequencing of the attP region demonstrated two major ORFs surrounding the predicted attP site and structural analysis of this region revealed a motif comprising three different inverted repeats surrounding a 12 bp palindrome. Analysis of the translated amino acid sequence upstream of the attP site demonstrated the presence of conserved residues found within integrase proteins of several temperate phages of different bacterial species.

17. **Genetic organization and functional analysis of a novel phage abortive infection system, AbiL, from *Lactococcus lactis*. Deng, Y. M., Liu, C. Q., Dunn, N. W. (1999). *Journal of Biotechnology* 67:135-149.** A plasmid-encoded phage abortive infection mechanism (AbiL) was identified from Lactococcus lactis biovar. diacetylactis LD10-1. AbiL conferred complete resistance to the small isometric-headed phage phi 712 (936 species) and partial resistance to the prolate-headed phage phi c2 (c2 species) when introduced into L. lactis LM0230. However, AbiL was not effective against the small isometric-headed phage ul36 (P335 species). The AbiL determinant was sequenced and it consists of two open reading frames, abiLi and abiLii. Their encoded proteins did not share significant homology with any known proteins in the protein databases. Transcriptional analysis indicated that abiLi and abiLii are organized as a single operon. Deletion within abiLii abolished the phage resistance. The levels of four phi c2-specific transcripts, three within the early transcribed region and one within the late transcribed region, were examined by RT-PCR, no effect of AbiL on synthesis of these transcripts was detected, suggesting that AbiL may act at a point after the transcription of phi c2 in L. lactis.

18. **Survival, physiology, and lysis of *Lactococcus lactis* in the digestive tract. Drouault, S. (1999). *Applied and Environmental Microbiology* 65:4881-4886.** The survival and the physiology of lactococcal cells in the different compartments of the digestive tracts of rats were studied in order to know better the fate of ingested lactic acid bacteria after oral administration. For this purpose, we used strains marked with reporter genes, the luxA-luxB gene of Vibrio harveyi and the gfp gene of Aequora victoria, that allowed us to differentiate the inoculated bacteria from food and the other intestinal bacteria. Luciferase was chosen to measure the metabolic activity of Lactococcus lactis in the digestive tract because it requires NADH, which is available only in metabolically active cells. The green fluorescent protein was used to assess the bacterial lysis independently of death. We report not only that specific factors affect the cell viability and integrity in some digestive tract compartments but also that the way bacteria are administrated has a dramatic impact. Lactococci which transit with the diet are quite resistant to gastric acidity (90 to 98% survival). In contrast, only 10 to 30% of bacteria survive in the duodenum. Viable cells are metabolically active in each compartment of the digestive tract, whereas most dead cells appear to be subject to rapid lysis. This property suggests that lactococci could be used as a vector to deliver specifically into the duodenum the proteins produced in the cytoplasm. This type of delivery vector would be particularly appropriate for targeting digestive enzymes such as lipase to treat pancreatic deficiencies.

19. **Integrity of powder-free examination gloves to bacteriophage penetration. Edlich, R. F. (1999). *J. Biomed. Mater. Res.* 48:755-758.** The purpose of this study was to compare the resistance to viral penetration of powder-free synthetic examination gloves with powder-free latex examination gloves commonly used in hospitals. Because these gloves had no holes, this study examined viral penetration through a membrane. Using a standard bacteriophage penetration model, no bacteriophage penetration was detected through the membrane for any of the gloves tested. The new powder-free nitrile and polyvinyl chloride synthetic examination gloves provided comparable resistance to viral penetration as did the powder-free latex examination gloves.

20. **Evaluation of reverse transcription-PCR and a bacteriophage-based assay for rapid phenotypic detection of rifampin resistance in clinical isolates of *Mycobacterium tuberculosis*. Eltringham, I. J. (1999). *J. Clin. Microbiol.* 37:3524-3527.** New rapid phenotypic assays for the detection of rifampin resistance in Mycobacterium tuberculosis have recently been described, but most of these require liquid cultures, which reduces the utility of many tests in terms of turnaround times. In the United Kingdom, over 90% of rifampin-resistant isolates are also resistant to isoniazid, so rifampin resistance can be used as a sensitive marker for multidrug-resistant tuberculosis. In this study, two new rapid phenotypic assays were compared to the standard resistance ratio method on 91 clinical isolates of M. tuberculosis. One, the phage amplified biologically (PhaB) assay, has been described previously and is based on the inability of susceptible isolates of M. tuberculosis to support the replication of bacteriophage D29 in the presence of inhibitory doses of rifampin. The other employed reverse transcription (RT)-PCR to demonstrate a reduction in inducible dnaK mRNA levels in susceptible isolates treated with rifampin. After incubation for 18 h with 4 g of rifampin per ml, the PhaB assay showed concordance with the resistance ratio method for 46 of 46 (100%) susceptible and 31 of 31 (100%) resistant isolates, while RT-PCR showed concordance for 46 of 48 (96%) susceptible and 35 of 36 (97%) resistant isolates. We believe these assays provide a reliable rapid means of susceptibility testing with a total turnaround time of only 48 h, although the PhaB assay is better in terms of its lower technical demand and cost and its applicability to tuberculosis susceptibility testing in developing countries.

21. **Evaluation of a bacteriophage-based assay (Phage amplified biologically assay) as a rapid screen for resistance to isoniazid, ethambutol, streptomycin, pyrazinamide, and ciprofloxacin among clinical isolates of *Mycobacterium tuberculosis*. Eltringham, I. J. (1999). *J. Clin. Microbiol.* 37:3528-3532.** Rapid molecular assays for the detection of mutations associated with rifampin resistance in Mycobacterium tuberculosis are commercially available. However, they are complex and expensive and have predictive values of 90 to 95%. Molecular assays for other drugs are less predictive of resistance. Ideally, assays based on phenotypic markers should be used for susceptibility testing, but these can take weeks to complete. We previously described a rapid phenotypic assay, the phage amplified biologically (PhaB) assay, for the rapid determination of rifampin and isoniazid susceptibility in clinical isolates of M. tuberculosis. In this study, we extended the assay to the study of ethambutol, pyrazinamide, streptomycin, and ciprofloxacin. After the optimization of antibiotic concentrations and incubation conditions, the assay was applied to each drug for a total of 157 isolates. The correlations between the results of the PhaB assay and the resistance ratio method were 94% for isoniazid, 96% for streptomycin, 100% for ciprofloxacin, 88% for ethambutol, and 87% for pyrazinamide. For ciprofloxacin, ethambutol, and pyrazinamide, significantly better correlations were found when a 90% reduction in plaque count was used as the cutoff. Turnaround times for the PhaB assay were 2 to 3 days, compared with 10 days for the resistance ratio method. We believe that this low-cost assay may have widespread applicability for the rapid screening of drug resistance in M. tuberculosis isolates, especially in developing countries.

22. **rexB of bacteriophage lambda is an anti-cell death gene. Engelberg-Kulka, H., Reches, M., Narasimhan, S., Schoulaker-Shwarz, R., Klemes, Y., Aizenman, E., Glaser, G. (1998).** ***Proceedings of the National Academy of Sciences, USA*** **95:15481-15486.** In Escherichia coli, programmed cell death is mediated through "addiction modules" consisting of two genes; the product of one gene is long-lived and toxic, whereas the product of the other is short-lived and antagonizes the toxic effect. Here we show that the product of lambdarexB, one of the few genes expressed in the lysogenic state of bacteriophage lambda, prevents cell death directed by each of two addiction modules, phd-doc of plasmid prophage P1 and the rel mazEF of E. coli, which is induced by the signal molecule guanosine 3',5'-bispyrophosphate (ppGpp) and thus by amino acid starvation. lambdaRexB inhibits the degradation of the antitoxic labile components Phd and MazE of these systems, which are substrates of ClpP proteases. We present a model for this anti-cell death effect of lambdaRexB through its action on the ClpP proteolytic subunit. We also propose that the lambdarex operon has an additional function to the well known phenomenon of exclusion of other phages; it can prevent the death of lysogenized cells under conditions of nutrient starvation. Thus, the rex operon may be considered as the "survival operon" of **phage** lambda.

23. **Epidemiology, genetics, and ecology of toxigenic** ***Vibrio cholerae*****. Faruque, S. M., Albert, M. J., Mekalanos, J. J. (1998).** ***Microbiology and Molecular Biology Reviews*** **62:1301-314.** Cholera caused by toxigenic Vibrio cholerae is a major public health problem confronting developing countries, where outbreaks occur in a regular seasonal pattern and are particularly associated with poverty and poor sanitation. The disease is characterized by a devastating watery diarrhea which leads to rapid dehydration, and death occurs in 50 to 70% of untreated patients. Cholera is a waterborne disease, and the importance of water ecology is suggested by the close association of V. cholerae with surface water and the population interacting with the water. Cholera toxin (CT), which is responsible for the profuse diarrhea, is encoded by a lysogenic bacteriophage designated CTXPhi. Although the mechanism by which CT causes diarrhea is known, it is not clear why V. cholerae should infect and elaborate the lethal toxin in the host. Molecular epidemiological surveillance has revealed clonal diversity among toxigenic V. cholerae strains and a continual emergence of new epidemic clones. In view of lysogenic conversion by CTXPhi as a possible mechanism of origination of new toxigenic clones of V. cholerae, it appears that the continual emergence of new toxigenic strains and their selective enrichment during cholera outbreaks constitute an essential component of the natural ecosystem for the evolution of epidemic V. cholerae strains and genetic elements that mediate the transfer of virulence genes. The ecosystem comprising V. cholerae, CTXPhi, the aquatic environment, and the mammalian host offers an understanding of the complex relationship between pathogenesis and the natural selection of a pathogen.

24. **Assessment of the effects of various UV sources on inactivation and photoproduct induction in phage T7 dosimeter. Fekete, A., Vink, A. A., Gaspar, S., Berces, A., Modos, K., Ronto, G., Roza, L. (1998).** ***PHOTOCHEMISTRY AND PHOTOBIOLOGY*** **68:527-531.** The correlation between the biologically effective dose (BED) of a phage T7 biological dosimeter and the induction of cyclobutane pyrimidine dimers (CPD) and (6-4) photoproducts ((6-4)PD) in the phage DNA was determined using seven various UV sources. The BED is the inactivation rate of phage T7 expressed in HT7 units. The CPD and (6-4)PD were determined by lesion-specific monoclonal antibodies in an immunodot-blot assay. The various lamps induced these lesions at different rates; the relative induction ratios of CPD to (6-4)PD increased with increasing effective wavelength of irradiation source. The amount of total adducts per phage was compared to the BED of phage T7 dosimeter, representing the average number of UV lesions in phage. For UVC (200-280 nm radiation) and unfiltered TL01 the number of total adducts approximates the reading; however, UV sources having longer effective wavelengths produced fewer CPD and (6-4)PD. A possible explanation is that although the most relevant lesions by UVC are the CPD and (6-4)PD, at longer wavelengths other photoproducts can contribute to the lethal damage of phages. The results emphasize the need to study the biological effects of solar radiation because the lesions responsible for the lethal effect may be different from those produced by various UV sources.

25. **Inducible prophages contribute to** ***Salmonella*** **virulence in mice. Figueroa-Bossi, N., Bossi, L. (1999).** ***Molecular Microbiology*** **33:167-176.** We show that Salmonella typhimurium harbours two fully functional prophages, Gifsy-1 and Gifsy-2, that can be induced by standard treatments or, more effectively, by exposing bacteria to hydrogen peroxide. Curing bacteria for the Gifsy-2 prophage significantly reduces Salmonella's ability to establish a systemic infection in mice. Cured strains recover their virulence properties upon relysogenization. **Phage** Gifsy-2 carries the sodC gene for a periplasmic [Cu,Zn]-superoxide dismutase previously implicated in the bacterial defences against killing by macrophages. The contribution of the Gifsy-1 prophage to virulence - undetectable in the presence of Gifsy-2 as prophage - becomes significant in cells that lack Gifsy-2 but carry the sodC gene integrated in the chromosome. This confirms the involvement of Gifsy-2-encoded SodC protein in Salmonella pathogenicity and suggests that the Gifsy-1 prophage carries one or more additional virulence genes that have a functional equivalent on the Gifsy-2 genome

26. **Genome structure of mycobacteriophage D29: implications for phage evolution. Ford, M. E., Sarkis, G. J., Belanger, A. E., Hendrix, R. W., Hatfull, G. F. (1998).** ***Journal of Molecular Biology*** **279:143-164.** Mycobacteriophage D29 is a lytic phage that infects both fast and slow-growing mycobacterial species. The complete genome sequence of D29 reveals that it is a close relative of the temperate mycobacteriophage L5, whose sequence has been described previously. The overall organization of the D29 genome is similar to that of L5, although a 3.6 kb deletion removing the repressor gene accounts for the inability of D29 to form lysogens. Comparison of the two genomes shows that they are punctuated by a large number of insertions, deletions, and substitutions of genes, consistent with the genetic mosaicism of lambdoid phages.

27. **Identification of four phage resistance plasmids from** ***Lactococcus lactis*** **subsp. cremoris HO2. Forde, A., Daly, C., Fitzgerald, G. F. (1999).** ***Applied and Environmental Microbiology*** **65:1540-1547.** The bacteriophage-host sensitivity patterns of 16 strains of Lactococcus lactis originally isolated from a mixed strain Cheddar cheese starter culture were determined. Using phages obtained from cheese factory whey, four of the strains were found to be highly phage resistant. One of these isolates, Lactococcus lactis subsp. cremoris HO2, was studied in detail to determine the mechanisms responsible for the phage insensitivity phenotypes. Conjugal transfer of plasmid DNA from strain HO2 allowed a function to be assigned to four of its six plasmids. A 46-kb molecule, designated pCI646, was found to harbor the lactose utilization genes, while this and plasmids of 58 kb (pCI658), 42 kb (pCI642), and 4.5 kb (pCI605) were shown to be responsible for the phage resistance phenotypes observed against the small isometric-headed phage phi712 (936 phage species) and the prolate-headed phage phic2 (c2 species). pCI658 was found to mediate an adsorption-blocking mechanism and was also responsible for the fluffy pellet phenotype of cells containing the molecule. pCI642 and pCI605 were both shown to be required for the operation of a restriction-modification system.

28. **Bacteriophage defence systems in lactic acid bacteria. Forde, A. (1999).** ***Antonie van Leeuwenhoek*** **76:89-113.** The study of the interactions between lactic acid bacteria and their bacteriophages has been a vibrant and rewarding research activity for a considerable number of years. In the more recent past, the application of molecular genetics for the analysis of phage-host relationships has contributed enormously to the unravelling of specific events which dictate insensitivity to bacteriophage infection and has revealed that while they are complex and intricate in nature, they are also extremely effective. In addition, the strategy has laid solid foundations for the construction of phage resistant strains for use in commercial applications and has provided a sound basis for continued investigations into existing, naturally-derived and novel, genetically-engineered defence systems. Of course, it has also become clear that phage particles are highly dynamic in their response to those defence systems which they do encounter and that they can readily adapt to them as a consequence of their genetic flexibility and plasticity. This paper reviews the exciting developments that have been described in the literature regarding the study of phage-host interactions in lactic acid bacteria and the innovative approaches that can be taken to exploit this basic information for curtailing phage infection.

29. **Sravnitel'noe izuchenie bakteriofagov** ***Morganella*** **i** ***Providencia*** **[Comparative study of** ***Morganella*** **and** ***Providencia*** **bacteriophages]. Gabrilovich, I. M., Zarochensev, M. V., Saimov, S. R. (1998).** ***Zhurnal Mikrobiologii, Epidemiologii i Immunobiologii*** **5:20-22.** 7 strains of M.morganii phages and 7 strains of P.rettgeri phages were isolated from lysogenic cultures and the environment. The main biological properties of these phages

were studied. The phages under study formed independent taxonomic groups. These phages were found to be highly specific and capable of being used for the identification of bacteria.

30. **Phage restriction and the presence of small plasmids in *Salmonella enteritidis*. Gado, I., Laszlo, V. G., Nagy, B., Milch, H., Drin, I., Awad-Masalmeh, M., Horvath, J. (1998). *Zentralblatt Fur Bakteriologie* 287:509-519.** Between 1990-1994, a total of 16,505 S. enteritidis strains of human, animal and food origin were phage-typed, using the Hungarian scheme and the changes of incidence of the dominant phage types were monitored. The incidence of PT1 (corresponding to Ward's PT1 was very high between 1990 and 1992 (67.9-71.0% of the total S. enteritidis isolates), later, it decreased. The prevalence of PT6 (corresponding to Ward's PT4) was rare until 1992, then it gradually increased. The phage type and plasmid content of 78 Salmonella enteritidis strains were determined. Small plasmids were present in 59% of the isolates, together with a serotype-specific (38 MDa) plasmid. A correlation was found between the presence of the small plasmid and phage restriction to two phages used for subdividing the Hungarian phage types 1 (PT1) and 6 (PT6) of S. enteritidis (corresponding to PT1 and PT4 in Ward's typing scheme, respectively).

31. **A species barrier between bacteriophages T2 and T4: exclusion, join-copy and join-cut-copy recombination and mutagenesis in the dCTPase genes. Gary, T. P., Colowick, N. E., Mosig, G. (1998). *Genetics* 148:1461-1473.** Bacteriophage T2 alleles are excluded in crosses between T2 and T4 because of genetic isolation between these two virus species. The severity of exclusion varies in different genes, with gene 56, encoding an essential dCT(D) Pase/dUT(D)Pase of these phages, being most strongly affected. To investigate reasons for such strong exclusion, we have (1) sequenced the T2 gene 56 and an adjacent region, (2) compared the sequence with the corresponding T4 DNA, (3) constructed chimeric phages in which T2 and T4 sequences of this region are recombined, and (4) tested complementation, recombination, and exclusion with gene 56 cloned in a plasmid and in the chimeric phages in Escherichia coli CR63, in which growth of wild-type T2 is not restricted by T4. Our results argue against a role of the dCTPase protein in this exclusion and implicate instead DNA sequence differences as major contributors to the apparent species barrier. This sequence divergence exhibits a remarkable pattern: a major heterologous sequence counter-clockwise from gene 56 (and downstream of the gene 56 transcripts) replaces in T2 DNA the T4 gene 69. Gene 56 base sequences bordering this substituted region are significantly different, whereas sequences of the dam genes, adjacent in the clockwise direction, are similar in T2 and in T4. The gene 56 sequence differences can best be explained by multiple compensating frameshifts and base substitutions, which result in T2 and T4 dCTPases whose amino acid sequences and functions remain similar. Based on these findings we propose a model for the evolution of multiple sequence differences concomitant with the substitution of an adjacent gene by foreign DNA: invasion by the single-stranded segments of foreign DNA, nucleated from a short DNA sequence that was complementary by chance, has triggered recombination-dependent replication by "join-copy" and "join-cut-copy" pathways that are known to operate in the T-even phages and are implicated in other organisms as well. This invasion, accompanied by heteroduplex formation between partially similar sequences, and perhaps subsequent partial heteroduplex repair, simultaneously substituted T4 gene 69 for foreign sequences and scrambled the sequence of the dCTPase gene 56. We suggest that similar mechanisms can mobilize DNA segments for horizontal transfer without necessarily requiring transposase or site-specific recombination functions.

32. **Roles of *Pseudomonas aeruginosa* las and rhl quorum-sensing systems in control of twitching motility. Glessner, A., Smith, R. S., Iglewski, B. H., Robinson, J. B. (1999). *Journal of Bacteriology* 181:1623-1629.** Pseudomonas aeruginosa is a ubiquitous environmental bacterium and an important human pathogen. The production of several virulence factors by P. aeruginosa is controlled through two quorum-sensing systems, las and rhl. We have obtained evidence that both the las and rhl quorum-sensing systems are also required for type 4 pilus-dependent twitching motility and infection by the pilus-specific phage D3112cts. Mutants which lack the ability to synthesize PAI-1, PAI-2, or both autoinducers were significantly or greatly impaired in twitching motility and in susceptibility to D3112cts. Twitching motility and phage susceptibility in the autoinducer-deficient mutants were partially restored by exposure to exogenous PAI-1 and PAI-2. Both twitching motility and infection by pilus-specific phage are believed to be dependent on the extension and retraction of polar type 4 pili. Western blot analysis of whole-cell lysates and enzyme-linked immunosorbent assays of intact cells were used to measure the amounts of pilin on the cell surfaces of las and rhl mutants relative to that of the wild type. It appears that PAI-2 plays a crucial role in twitching motility and phage infection by affecting the export and assembly of surface type 4 pili. The ability of P. aeruginosa cells to adhere to human bronchial epithelial cells was also found to be dependent on the rhl quorum-sensing system. Microscopic analysis of twitching motility indicated that mutants which were unable to synthesize PAI-1 were defective in the maintenance of cellular monolayers and migrating packs of cells. Thus, PAI-1 appears to have an essential role in maintaining cell-cell spacing and associations required for effective twitching motility.

33. **Metastabil'nost' fenotipa u bakterii [Metastable phenotype of bacteria]. Golovlev, E. L. (1998). *Mikrobiologica* 67:149-155.** This review analyzes data available in the literature and the author's own data on the phenotypic variability of bacteria that occurs within the framework of a genotype unchanging in terms of the genetic information stored. This variability is a form of bacterial adaptation to an unstable environment and results from a specific form of natural selection. This phenomenon arose evolutionarily not as a mechanism to provide genetic diversity for the divergence process but as a mechanism of species stabilization; therefore, it was termed phenotype metastability. It includes, as specific variants, processes known as phase and antigenic variations, R-S-M dissociation, phenotype conversion, etc. The mechanisms of phenotype metastability are extremely diverse. They include alternative expression (of the switch on-switch off type) of individual genes or small groups of genes; variation in the composition of synthesized proteins controlled at the level of transcription; expression of complex phenotypes adapted to different environmental conditions that involves phage transposition, reading-frame-shift mutations, etc. The phenomenon of phenotype metastability is widespread among bacteria.

34. **The use of a fluorescent bacteriophage assay for detection of *Escherichia coli* O157:H7 in inoculated ground beef and raw milk. Goodridge, L., Chen, J., Griffiths, M. (1999). *International Journal of Food Microbiology* 47:43-50.** The objective of this study was to develop a fluorescent bacteriophage assay (FBA) for the detection of E. coli O157:H7 in ground beef and raw milk. The FBA is a two step assay that combines immunomagnetic separation, to separate the target organism from mixed culture, with a highly specific fluorescently stained bacteriophage to label the E. coli O157:H7 cells. When used in conjunction with flow cytometry, the FBA was able to detect 2.2 CFU/g of artificially contaminated ground beef following a 6 h enrichment. Between 10 (1) and 10(2) CFU/ml of artificially contaminated raw milk were detectable after a 10 h enrichment step. The results show that the FBA is potentially useful as a rapid technique for the preliminary detection of E. coli O157:H7 in food.

35. **Development and characterization of a fluorescent-bacteriophage assay for detection of *Escherichia coli* O157:H7. Goodridge, L., Chen, J., Griffiths, M. (1999). *Applied and Environmental Microbiology* 65:1397-1404.** In this paper we describe evaluation and characterization of a novel assay that combines immunomagnetic separation and a fluorescently stained bacteriophage for detection of Escherichia coli O157:H7 in broth. When it was combined with flow cytometry, the fluorescent-bacteriophage assay (FBA) was capable of detecting 10(4) cells/ml. A modified direct epifluorescent-filter technique (DEFT) was employed in an attempt to estimate bacterial concentrations. Using regression analysis, we calculated that the lower detection limit was between 10 (2) and 10(3) cells/ml; however, the modified DEFT was found to be an unreliable method for determining bacterial concentrations. The results of this study show that the FBA, when combined with flow cytometry, is a sensitive technique for presumptive detection of E. coli O157:H7 in broth cultures.

36. **Bacteriophage and associated polysaccharide depolymerases--novel tools for study of bacterial biofilms [published erratum appears in J Appl Microbiol 1999 Feb;86(2):359]. Hughes, K. A., Sutherland, I. W., Clark, J., Jones, M. V. (1998). *Journal of Applied Microbiology* 85:583-590.** Bacteriophage for three representative strains of Gram-negative biofilm bacteria have proved to be of widespread occurrence. Lytic bacteriophage have been isolated from local sewage for the bacterium 1.15, an exopolysaccharide (EPS)-producing pseudomonad found originally as a component of biofilms in a local river, and for two Enterobacter agglomerans strains from industrial biofilms. Representative examples of all three bacteriophage possess a relatively low burst

size and on solid media, exhibit very large plaques surrounded by a wide halo (5-20 mm) indicative of polysaccharide depolymerase action. The bacteriophage are thus similar to other viruses for EPS-producing bacteria in inducing the synthesis of enzymes degrading the polymers which occlude the bacterial cell surface. In each preparation, the polysaccharase activity was associated both with sedimented phage particles and with the supernate of bacterial lysates. The enzymes have been partially purified and used to prepare polysaccharide digests in which the major products from each polysaccharide are the presumed repeat units of the polymers or oligomers of these. The soluble phage enzymes each degrade their substrate by acting as endo-glycanohydrolases. The phage and their associated enzymes thus provide very useful highly specific tools for studies of biofilms incorporating the bacterial host strains. Their potential applications in studies on bacterial biofilms are discussed.

37. **Targeted delivery of multivalent phage display vectors into mammalian cells. Ivanenkov, V., Felici, F., Menon, A. G. (1998). *Biochimica et Biophysica Acta* 1448:463-472.** Novel peptide motives targeting endocytosing receptors were isolated from phage display libraries of random peptides by recovering internalized phage from mammalian cells. The peptide-presenting phage selected by internalization in HEp-2 and ECV304 human cells were taken up 1000- to 100,000-fold more efficiently than their parent libraries, and from 10 to 100 times faster than phage particles displaying integrin-binding peptides. A high degree of selectivity of phage uptake was observed in these cells: phage selected in ECV304 cells were internalized approximately 100-fold more efficiently in ECV304 cells than in HEp-2 cells. Likewise, phage selected in HEp-2 cells were subsequently taken up approximately 40-fold more efficiently by HEp-2 cells than by ECV304 cells. In multiple independent trials using a cyclic peptide library, an identical peptide sequence displayed on phage was internalized by and recovered from ECV304 cells. These findings indicate that the internalization process is highly selective, and is capable of capturing a specific peptide from 2 x 10(7) peptide variants. Immunofluorescence microscopy showed juxtanuclear localization of internalized phage. These results demonstrate the feasibility of using multivalent phage-display libraries to identify new targeting ligands for the intracellular delivery of macromolecules.

38. **Uptake and intracellular fate of phage display vectors in mammalian cells. Ivanenkov, V., Felici, F., Menon, A. G. (1998). *Biochimica et Biophysica Acta* 1448:450-462.** Receptor-mediated endocytosis is exploited in experimental systems for selective delivery of genes and drugs into specific cells. To improve targeting efficiency of delivery vectors, we have used phage display technology to isolate novel ligands for endocytosed receptors. We show here that phage vectors internalized by mammalian cells via integrin-mediated endocytosis can be rescued by cell lysis and quantitated by infection of bacteria. Immediately following uptake, phage enter an intracellular compartment where they remain intact, with phage titer unaffected by the addition of chloroquine. Phage are then translocated to a second intracellular compartment in which they are inactivated and their titer affected by chloroquine. Immunofluorescence microscopy showed an association of the second compartment with supranuclear organelles. The ability to recover internalized phage in an infectious form from two distinctive intracellular compartments provides a means to select novel ligands from phage libraries for targeted delivery of macromolecules into mammalian cells.

39. **A bacteriophage encoding a pathogenicity island, a type-IV pilus and a phage receptor in cholera bacteria [see comments]. Karaolis, D. K., Somara, S., Maneval, D. R. Jr., Johnson, J. A., Kaper, J. B. (1999). *Nature (London)* 399:375-379.** The virulence properties of many pathogenic bacteria are due to proteins encoded by large gene clusters called pathogenicity islands, which are found in a variety of human pathogens including Escherichia coli, Salmonella, Shigella, Yersinia, Helicobacter pylori, Vibrio cholerae, and animal and plant pathogens such as Dichelobacter nodosus and Pseudomonas syringae. Although the presence of pathogenicity islands is a prerequisite for many bacterial diseases, little is known about their origins or mechanism of transfer into the bacterium. The bacterial agent of epidemic cholera, Vibrio cholerae, contains a bacteriophage known as cholera-toxin phage (CTXphi), which encodes the cholera toxin, and a large pathogenicity island called the VPI (for V. cholerae pathogenicity island) which itself encodes a toxin-coregulated pilus that functions as a colonization factor and as a CTXphi receptor. We have now identified the VPI pathogenicity island as the genome of another filamentous bacteriophage, VPIphi. We show that VPIphi is transferred between V. cholerae strains and provide evidence that the TcpA subunit of the toxin-coregulated type IV pilus is in fact a coat protein of VPIphi. Our results are the first description of a phage that encodes a receptor for another phage and of a virus-virus interaction that is necessary for bacterial pathogenicity.

40. **Genetic homogeneity and phage susceptibility of ruminal strains of *Streptococcus bovis* isolated in Australia. Klieve, A. V., Heck, G. L., Prance, M. A., Shu, Q. (1999). *Letters in Applied Microbiology* 29:108-112.** The genetic homogeneity of 37 strains of ruminal streptococci was investigated by comparing DNA fragment profiles on agarose gels following restriction endonuclease digestion with Hae III, Cfo I and Msp I. Thirty strains were indistinguishable from Streptococcus bovis strains, 2B, H24 and AR3. The remaining three strains were similar but not identical to a ruminal strain of Strep. intermedius (AR36). In addition, the susceptibility of these strains to infection by five bacteriophages was examined. Three of the phages (phi Sb02, phi Sb03 and phi Sb04) were specific to the strain of Strep. bovis from which they were isolated, while phages 2BV and phi Sb01 infected one and two strains, respectively, in addition to their primary host. It was concluded that although Strep. bovis is relatively homogeneous genetically, broad host range phages appear to be uncommon with this bacterial species.

41. **The hunt is on for new ways to overcome bacterial resistance. Knudson, M. (1998). *Technology Review* 100:22-30?** Researchers from various pharmaceutical companies are employing high technology approaches to develop ways to address disease-causing microbes that mutate to resist conventional antibiotics.

42. **Soderzhanie mikroorganizmov na ottiskakh posle dezinfektsii ikh metodom pogruzheniia v rastvory gipokhlorita natriia [The microorganism count on impressions after their disinfection by submersion in sodium hypochlorite solutions]. Koshmanova, T. N., Panteleeva, L. G. (1998). *Stomatologiia* 77:48-49.** The virucidal, bactericidal, and fungicidal activity of sodium hypochlorite is studied with silicone imprints. Poliomyelitis virus (type I vaccine strain Sabin LSc 2 ab with titer 10(7.36) TCD50/ml), bacteriophage f52 with titer 2.10(7) PFU/ml, Staphylococcus aureus strain 906, and Candida albicans in concentrations 10(7) corpuscles/ml in the presence of protein die completely in 20 min when submerged in 0.5% sodium hypochlorite solution. Imprints from alginate materials are destroyed if submerged in this solution.

43. **Biocontrol of *Escherichia coli* O157 with O157-specific bacteriophages. Kudva, I. T. (1999). *Applied and Environmental Microbiology* 65:3767-3773.** Escherichia coli O157 antigen-specific bacteriophages were isolated and tested to determine their ability to lyse laboratory cultures of Escherichia coli O157:H7. A total of 53 bovine or ovine fecal samples were enriched for phage, and 5 of these samples were found to contain lytic phages that grow on E. coli O157:H7. Three bacteriophages, designated KH1, KH4, and KH5, were evaluated. At 37 or 4 degrees C, a mixture of these three O157-specific phages lysed all of the E. coli O157 cultures tested and none of the non-O157 E. coli or non-E. coli cultures tested. These results required culture aeration and a high multiplicity of infection. Without aeration, complete lysis of the bacterial cells occurred only after 5 days of incubation and only at 4 degrees C. Phage infection and plaque formation were influenced by the nature of the host cell O157 lipopolysaccharide (LPS). Strains that did not express the O157 antigen or expressed a truncated LPS were not susceptible to plaque formation or lysis by phage. In addition, strains that expressed abundant mid-range-molecular-weight LPS did not support plaque formation but were lysed in liquid culture. Virulent O157 antigen-specific phages could play a role in biocontrol of E. coli O157:H7 in animals and fresh foods without compromising the viability of other normal flora or food quality.

44. **Targeting bacteriophage to mammalian cell surface receptors for gene delivery. Larocca, D., Witte, A., Johnson, W., Pierce, G. F., Baird, A. (1998). *Human Gene Therapy* 9:2393-2399.** Filamentous bacteriophages represent one of nature's most elegant ways of packaging and delivering DNA. In an effort to develop novel methods for ligand discovery via phage gene delivery, we conferred mammalian cell tropism to filamentous bacteriophages by attaching basic fibroblast growth factor (FGF2), transferrin, or epidermal growth factor (EGF) to their coat proteins and measuring CMV promoter-driven

reporter gene expression in target cells. In this system, FGF2 was a more effective targeting agent than transferrin or EGF. The detection of green fluorescent protein (GFP) or beta-galactosidase (beta-Gal) activity in cells required FGF2 targeting and was phage concentration dependent. Specificity of the targeting for high-affinity FGF receptors was demonstrated by competing the targeted phage with FGF2, by the failure of FGF2-targeted bacteriophage to transduce high-affinity FGF receptor-negative cells, and by their ability to transduce these same cells when stably transfected with FGFR1, a high-affinity FGF receptor. Long-term transgene expression was established by selecting colonies for G418 resistance, suggesting that with the appropriate targeted tropism, filamentous bacteriophage can serve as a vehicle for targeted gene delivery to mammalian cells.

45. **Gene transfer to mammalian cells using genetically targeted filamentous bacteriophage. Larocca, D., Kassner, P. D., Witte, A., Ladner, R. C., Pierce, G. F., Baird, A. (1999). *FASEB Journal* 13:727-734.** We have genetically modified filamentous bacteriophage to deliver genes to mammalian cells. In previous studies we showed that noncovalently attached fibroblast growth factor (FGF2) can target bacteriophage to COS-1 cells, resulting in receptor-mediated transduction with a reporter gene. Thus, bacteriophage, which normally lack tropism for mammalian cells, can be adapted for mammalian cell gene transfer. To determine the potential of using phage-mediated gene transfer as a novel display phage screening strategy, we transfected COS-1 cells with phage that were engineered to display FGF2 on their surface coat as a fusion to the minor coat protein, pIII. Immunoblot and ELISA analysis confirmed the presence of FGF2 on the phage coat. Significant transduction was obtained in COS-1 cells with the targeted FGF2-phage compared with the nontargeted parent phage. Specificity was demonstrated by successful inhibition of transduction in the presence of excess free FGF2. Having demonstrated mammalian cell transduction by phage displaying a known gene targeting ligand, it is now feasible to apply phage-mediated transduction as a screen for discovering novel ligands.

46. **Rekonstruktsiia vozmozhnykh putei proiskhozhdeniia i morfologicheskoi evoliutsii bakteriofagov [Reconstruction of possible paths of the origin and morphological evolution of bacteriophages]. Letarov, A. V. (1999). *Genetika* 34:1461-1469.** The problem of the origin and evolution of viruses and, in particular, the origin and evolution of bacteriophages is of considerable interest. However, so far, this problem has not been solved with quantitative methods of molecular systematics. In the present study, an attempt to reconstruct the possible paths of appearance and evolution of bacteriophages based on their structural features and morphogenesis, as well as general characteristics of their life cycles and genome organization, was carried out. A scheme describing phylogeny of the main bacteriophage groups and evolution of their life cycles is suggested. Existence of two independently evaluating types of morphogenesis ("budding outward" and "budding inward") is postulated.

47. **An evolutionary link between sporulation and prophage induction in the structure of a repressor:anti-repressor complex. Lewis, R. J., Brannigan, J. A., Offen, W. A., Smith, I., Wilkinson, A. J. (1998). *Journal of Molecular Biology* 283:907-912.** Spore formation is an extreme response of some bacteria to adversity. In Bacillus subtilis the proteins of the sin, sporulation inhibition, region form a component of an elaborate molecular circuitry that regulates the commitment to sporulation. SinR is a tetrameric repressor protein that binds to the promoters of genes essential for entry into sporulation and prevents their transcription. This repression is overcome through the activity of SinI, which disrupts the SinR tetramer through the formation of a SinI-SinR heterodimer. The interactions governing this curious quaternary transition are revealed in the crystal structure of the SinI-SinR complex. The most striking, and unexpected, finding is that the tertiary structure of the DNA-binding domain of SinR is identical with that of the corresponding domains of the repressor proteins, CI and Cro, of bacteriophage 434 that regulate lysis/lysogeny. This structural similarity greatly exceeds that between SinR and any bacterial protein or between the 434 repressor proteins and their homologues in the closely related bacteriophage lambda. The close evolutionary relationship implied by the structures of SinR and the 434 repressors provokes both comparison of their functions and a speculative consideration of the intriguing possibility of an evolutionary link between the two adaptive responses, sporulation and prophage induction.

48. **A new and simple method for concentration of enteric viruses from water. Li, J. W., Wang, X. W., Rui, Q. Y., Song, N., Zhang, F. G., Ou, Y. C., Chao, F. H. (1998). *Journal of Virological Methods* 74:99-108.** A new type of electropositive filter media particle was tested to adsorb bacteriophage f2 and enteric viruses from tap water. 3 x nutrient broth (pH 7.2) was used to elute the adsorbed viruses, and the eluate was reconcentrated by polyethylene glycol (Mw 6000) precipitation with a final concentration of 10% (wt./vol.). The adsorption of bacteriophage was reliable and efficient, and not affected by the pH value, temperature, turbidity and organic materials in water. This method gave a recovery of Polio 1 virus 96.0% for small-volume tap water; 88.7% for large-volume water; and gave a comparable recovery of HAV, Coxsackie B3 and Echo 7 from tap water. The concentration method need not acidify virus-containing water, add exogenous multivalent cation salts, or require expensive equipment.

49. **Defektnye fagi kak faktor antagonizma u blizkorodstvennykh batsill [Defective pages as an antagonistic factor in closely-related bacilli]. Lotareva, O. V., Prozorov, A. A. (1999). *Mikrobiologica* 67:788-791.** The antagonistic effect produced by the detective phage PBSX during cocultivation of the mutant strain B. subtilis 168, in which this phage is heat-inducible, and strain B. subtilis NRS231, which also bears a defective phage, was investigated. As soon as in the first hours of cocultivation under conditions of PBSX induction, the number of viable cells of strain NRS231 decreased by two orders of magnitude. However, the effect was not observed if the temperature of cocultivation was noninducing. The results confirm the supposition that defective phages may play a role in the competition between closely related bacilli.

50. **Comparative genomics of *Streptococcus thermophilus* phage species supports a modular evolution theory. Lucchini S, Desiere, F., Brussow, H. (1999). *Journal of Virology* 73:8647-8656.** The comparative analysis of five completely sequenced Streptococcus thermophilus bacteriophage genomes demonstrated that their diversification was achieved by a combination of DNA recombination events and an accumulation of point mutations. The five phages included lytic and temperate phages, both pac site and cos site, from three distinct geographical areas. The units of genetic exchange were either large, comprising the entire morphogenesis gene cluster, excluding the putative tail fiber genes, or small, consisting of one or maximally two genes or even segments of a gene. Many indels were flanked by DNA repeats. Differences in a single putative tail fiber gene correlated with the host ranges of the phages. The predicted tail fiber protein consisted of highly conserved domains containing conspicuous glycine repeats interspersed with highly variable domains. As in the T-even coliphage adhesins, the glycine-containing domains were recombinational hot spots. Downstream of a highly conserved DNA replication region, all lytic phages showed a short duplication; in three isolates the origin of replication was repeated. The lytic phages could conceivably be derived from the temperate phages by deletion and multiple rearrangement events in the lysogeny module, giving rise to occasional selfish phages that defy the superinfection control systems of the corresponding temperate phages.

51. **Resistance of *Pseudomonas aeruginosa* PAO1 phage F116 to sodium hypochlorite. Maillard, J.-Y., Hann, A. C., Perrin, R. (1998). *Journal of Applied Microbiology* 85:799-806.** The development of viral resistance to sodium hypochlorite was investigated using the Pseudomonas aeruginosa bacteriophage F116 as a model system. This phage was chosen because of its structural characteristics and former investigations conducted in this laboratory. F116 was shown to be sensitive to a sodium hypochlorite concentration of 0.0075 gl-1 (available chlorine) which produced a 5 log10 reduction in titre in a suspension test. Survival bacteriophages challenged with this sodium hypochlorite concentration were isolated, propagated and challenged again with the same and higher concentrations of the biocide. It was observed that progeny virions were becoming increasingly resistant to sodium hypochlorite challenges up to a concentration of 0.0175 gl-1 of available chlorine. It was also noticed that 1-2 log10 of F116 virions from resistant phage lysates remained sensitive to the biocide. An electron microscopical investigation of F116 resistant lysates showed that the phage resistance to sodium hypochlorite was not caused by F116 particles aggregation. Furthermore, no morphological difference between the sensitive and resistant F116 particles to sodium hypochlorite was identified.

52. **Major capsid proteins of certain *Vibrio* and *Aeromonas* phages are homologous to the equivalent protein, gp23(*), of coliphage T4. Matsuzaki, S., Kuroda, K., Kimura, S., Tanaka, S. (1999). *Archives of Virology* 144:1647-1651.** N-terminal amino acid sequences of major capsid proteins (Mcps)

of three vibriophages (KVP20, KVP40 and nt-1), two aeromonad phages (Aeh 1 and 65) and coliphage T4 were compared. All these phages are morphologically similar, belonging to family Myoviridae and the vernacular genus name "T4-like phages". A dendrogram constructed from homology data indicated that (i) the three vibriophages were closely related, (ii) the two aeromonad phages were also fairly related and (iii) these five phages were all distantly, but definitely, related to coliphage T4. These results suggest that Mcps of morphologically similar phages are highly conserved and may serve as a measure to assess the phylogenetic relationships among different phages of similar morphology.

53. **Protective effects of bacteriophage on experimental *Lactococcus garvieae* infection in yellowtail. Nakai, T., Sugimoto, R., Park, K.-H., Matsuoka, S., Mori, K., Nishioka, T., Maruyama, K. (1999). *Diseases of Aquatic Organisms* 37:33-41.** The present study describes the *in vitro* and *in vivo* survival of *Lactococcus garvieae* bacteriophages and the potential of the phage for controlling experimental *L. garvieae* infection in yellowtail. Anti-*L. garvieae* phages persisted well in various physicochemical (water temperature, salinity, pH) and biological (feed, serum and alimentary tract extracts of yellowtail) conditions, except for low acidity. In the *in vivo*, the phage PLgY-16 was detected in the spleens of yellowtail until 24 h after intraperitoneal (i.p.) injection, or the phage was recovered from the intestine of yellowtail 3 h after the oral administration of phage-impregnated feed but undetectable 10 h later. Simultaneous administration of live *L. garvieae* and phage enhanced recovery of the phage from the spleen or intestine. The survival rate was much higher in yellowtail that received i.p. injection of the phage after i.p. challenge with *L. garvieae*, compared with that of control fish without phage injection. When fish were i.p.-injected with phage at different hours after *L. garvieae* challenge, higher protective effects were demonstrated in fish that received phage treatment at the earlier time. Protection was also obtained in yellowtail receiving phage-impregnated feed, in which fish were challenged by an anal intubation with *L. garvieae*. Anal-intubated *L. garvieae* were detected constantly in the spleens of the control fish, while they were detected sporadically and disappeared from the phage-treated fish 48 h later. On the other hand, orally administered phage was detected at high plaque-forming units from the intestines and spleens of the phage-treated fish until 48 h later. These results indicate that intraperitoneally or orally administered anti-*L. garvieae* phage prevented fish from experimental *L. garvieae* infection, suggesting potential use of the phage for controlling the disease.

54. **A filamentous phage of *Vibrio parahaemolyticus* O3:K6 isolated in Laos. Nakasome, N., Ikema, M., Higa, N., Yamashiro, T., Iwanaga, M. (1999). *MICROBIOLOGY AND IMMUNOLOGY* 43:385-388.** A filamentous phage, 'lvpf5,' of Vibrio parahaemolyticus O3:K6 strain LVP5 was isolated and characterized. The host range was not restricted to serotype O3:K6, but 7 of 99 V. parahaemolyticus strains with a variety of serotypes were susceptible to the phage. The phage was inactivated by heating at 80 C for 10 min and by treating with chloroform. Sodium dodecyl sulfate-polyacrylamide gel electrophoresis of the phage exhibited a 3.8 kDa protein. The amino-terminal amino acid sequence of the coat protein was determined as AEGGAADPFEAIDLLGVATL. The phage genome consisted of a single-stranded DNA molecule. The activity of the phages was inhibited by anti-Na2 pili antibody.

55. **The complete nucleotide sequence of phi CTX, a cytotoxin-converting phage of *Pseudomonas aeruginosa*: implications for phage evolution and horizontal gene transfer via bacteriophages. Nakayama, K., Kanaya, S., Ohnishi, M., Terawaki, Y., Hayashi, T. (1999). *Molecular Microbiology* 31:399-419.** phi CTX is a cytotoxin-converting phage isolated from Pseudomonas aeruginosa. In this study, we determined the complete nucleotide sequence of the phi CTX phage genome. The precise genome size was 35,538 bp with 21 base 5'-extruding cohesive ends. Forty-seven open reading frames (ORFs) were identified on the phi CTX genome, including two previously identified genes, ctx and int. Among them, 15 gene products were identified in the phage particle by protein microsequencing. The most striking feature of the phi CTX genome was an extensive homology with the coliphage P2 and P2-related phages; more than half of the ORFs (25 ORFs) had marked homology to P2 genes with 28.9-65.8% identity. The gene arrangement on the genome was also highly conserved for the two phages, although the G + C content and codon usage of most phi CTX genes were similar to those of the host P. aeruginosa chromosome. In addition, phi CTX was found to share several common features with P2, including the morphology, non-inducibility, use of lipopolysaccharide core oligosaccharide as receptor and Ca(2+)-dependent receptor binding. These findings indicate that phi CTX is a P2-like phage well adapted to P. aeruginosa, and provide clear evidence of the intergeneric spread and evolution of bacteriophages. Furthermore, comparative analysis of genome structures of phi CTX, P2 and other P2 relatives revealed the presence of several hot-spots where foreign DNAs, including the cytotoxin gene, were inserted. They appear to be deeply concerned in the acquisition of various genes that are horizontally transferred by bacteriophage infection.

56. **Phage viability in organic media: insights into phage stability. Olofsson, L., Ankarloo, J., Nicholls, I. A. (1999). *Journal of Molecular Recognition* 11:91-93.** The stability of the filamentous phages derived from phagemid pG8H6 has been examined in a range of solvents and solvent mixtures. The results show an enhanced capacity to infect E. coli after exposure to various organic solvent-water mixtures. The dependence of stability upon solvent hydrophobicity was demonstrated. Furthermore, conditions have been identified which should allow the application of phage display libraries based upon pG8H6 in organic media.

57. **Poor efficacy of residual chlorine disinfectant in drinking water to inactivate waterborne pathogens in distribution systems. Payment, P. (1999). *Can. J. Microbiol.* 45:709-715.** To evaluate the inactivating power of residual chlorine in a distribution system, test microorganisms (Escherichia coli, Clostridium perfringens, bacteriophage phi-X 170, and poliovirus type 1) were added to drinking water samples obtained from two water treatment plants and their distribution system. Except for Escherichia coli, microorganisms remained relatively unaffected in water from the distribution systems tested. When sewage was added to the water samples, indigenous thermotolerant coliforms were inactivated only when water was obtained from sites very close to the treatment plant and containing a high residual chlorine concentration. Clostridium perfringens was barely inactivated, suggesting that the most resistant pathogens such as Giardia lamblia, Cryptosporidium parvum, and human enteric viruses would not be inactivated. Our results suggest that the maintenance of a free residual concentration in a distribution system does not provide a significant inactivation of pathogens, could even mask events of contamination of the distribution, and thus would provide only a false sense
of safety with little active protection of public health. Recent epidemiological studies that have suggested a significant waterborne level of endemic gastrointestinal illness could then be explained by undetected intrusions in the distribution system, intrusions resulting in the infection of a small number of individuals without eliciting an outbreak situation.

58. **Targeted gene delivery to mammalian cells by filamentous bacteriophage. Poul, W. A., Marks, J. D. (1999). *Journal of Molecular Biology* 288:203-211.** We report that prokaryotic viruses can be re-engineered to infect eukaryotic cells resulting in expression of a reporter gene inserted into the bacteriophage genome. Phage capable of binding mammalian cells expressing the growth factor receptor ErbB2 and undergoing receptor-mediated endocytosis were isolated by selection of a phage antibody library on breast tumor cells and recovery of infectious phage from within the cell. As determined by immunofluorescence, F5 phage were efficiently endocytosed into 100 % of ErbB2 expressing SKBR3 cells. To achieve reporter gene expression, F5 phage were engineered to package the green fluorescent protein (GFP) reporter gene driven by the CMV promoter. These phage when applied to cells underwent ErbB2-mediated endocytosis leading to GFP expression. GFP expression occurred only in cells overexpressing ErbB2, was dose-dependent reaching, 4 % of cells after 60 hours and was detected with phage titers as low as 2.0 x 10(7) cfu/ml (500 phage/cell). The results demonstrate that bacterial viruses displaying the appropriate antibody can bind to mammalian receptors and utilize the endocytic pathway to infect eukaryotic cells, resulting in expression of a reporter gene inserted into the viral genome. This represents a novel method to discover targeting molecules capable of delivering a gene intracellularly into the correct trafficking pathway for gene expression by directly screening phage antibodies. This should significantly facilitate the identification of appropriate targets and targeting molecules for gene therapy or other applications where delivery into the cytosol is required. This approach can be adapted to directly select, rather than screen, phage antibodies for targeted gene expression. The results also demonstrate the potential of phage antibodies as an in vitro or in vivo targeted gene delivery vehicle.

59. **Inactivation of *Lactobacillus helveticus* bacteriophages by thermal and chemical treatments. Quiberoni, A. (1999). *J. Food. Prot.* 62:894-898.** The effect of several biocides and thermal treatments on the viability of four Lactobacillus helveticus phages was investigated. Times to achieve 99% inactivation of phages at 63 degrees C and 72 degrees C in three suspension media were calculated. The three suspension media were tris magnesium gelatin buffer (10 mM Tris-HCl, 10 mM MgSO4, and 0.1% wt/vol gelatin), reconstituted skim milk sterile reconstituted commercial nonfat dry skim milk, and Man Rogosa Sharpe broth. The thermal resistance depended on the phage considered, but a treatment of 5 min at 90 degrees C produced a total inactivation of high titer suspensions of all phages studied. The results obtained for the three tested media did not allow us to establish a clear difference among them, since some phages were more heat resistant in Man Rogosa Sharpe broth and others in tris magnesium gelatin buffer. From the investigation on biocides, we established that sodium hypochlorite at a concentration of 100 ppm was very effective in inactivating phages. The suitability of ethanol 75%, commonly used to disinfect utensils and laboratory equipment, was confirmed. Isopropanol turned out to be, in general, less effective than ethanol at the assayed concentrations. In contrast, peracetic acid (0.15%) was found to be an effective biocide for the complete inactivation of all phages studied after 5 min of exposure. The results allowed us to establish a basis for adopting the most effective thermal and chemical treatments for inactivating phages in dairy plant and laboratory environments.

60. **Model for bacteriophage T4 development in *Escherichia coli*. Rabinovitch, A., Hadas, H., Einav, M., et al. (1999). *Journal of Bacteriology* 181:1677-1683.** Mathematical relations for the number of mature T4 bacteriophages, both inside and after lysis of an Escherichia coli cell, as a function of time after infection by a single phage were obtained, with the following five parameters: delay time until the first T4 is completed inside the bacterium (eclipse period, nu) and its standard deviation (sigma), the rate at which the number of ripe T4 increases inside the bacterium during the rise period (alpha), and the time when the bacterium bursts (mu) and its standard deviation (beta). Burst size [B = alpha(mu - nu)], the number of phages released from an infected bacterium, is thus a dependent parameter. A least-squares program was used to derive the values of the parameters for a variety of experimental results obtained with wild-type T4 in E. coli B/r under different growth conditions and manipulations (H. Hadas, M. Einav, I. Fishov, and A. Zaritsky, Microbiology 143:179-185, 1997). A "destruction parameter" (zeta) was added to take care of the adverse effect of chloroform on phage survival. The overall agreement between the model and the experiment is quite good. The dependence of the derived parameters on growth conditions can be used to predict phage development under other experimental manipulations.

61. **RecA-dependent viral burst in bacterial colonies during the entry into stationary phase. Ramirez, E., Schmidt, M., Rinas, U., Villaverde, A. (1999). *FEMS Microbiology Letters* 170:313-317.** We have explored the nature of the sudden viral amplification observed during the ageing of P22-infected lysogenic colonies of Salmonella typhimurium [Ramirez, E, and Villaverde, A. (1997) Gene 202, 147-149]. By a comparative analysis of the wild-type P22 and a P22 integration mutant, it has been shown that the conditions promoting prophage induction occur in only a small portion of the bacterial population and briefly during the transition between the exponential growth and the stationary phase. The viral burst is RecA-dependent and cannot be reproduced in continuous culture by a mere decrease of the growth rate. This suggests that the limited viral propagation in colonies is probably linked to heterogeneous physiological conditions within colonial populations, distinct from those of the homogeneous liquid cultures.

62. **Susceptibility of bacteria in estuarine environments to autochthonous bdellovibrios. Rice, T. D., Williams, H. N., Turng, B. F. (1998). *Microbial Ecology* 35:256-264.** Members of the genus *Bdellovibrio* exist as obligate predators of other gram-negative bacilli. They are believed to require large numbers of prey bacteria ($>10^4$ ml^{-1}) to survive. Although prey bacteria are essential to the survival of bdellovibrio populations, and to studies of the predator's role in nature, the number of bdellovibrio-susceptible bacteria in environmental samples has not been investigated. This study quantified bacteria that were susceptible to predation by the bdellovibrios. Bacteria recovered from water, sediment, and oyster-shell surface epibiota at various sites in the Chesapeake Bay system were tested for their susceptibility to bdellovibrios collected from homologous sites. The mean number (log_{10}) of susceptible bacterial colonies recovered by culture was 3.33 ml^{-1} in water, 4.14 ml^{-1} in sediment and 5.76 ml^{-1} from oyster shells. Seventy three to 85% of all isolates tested were susceptible to bdellovibrios. Considering the actual number of bacteria in most environments is estimated to be 100 to 1000-fold greater than measured by culturing, the number of bdellovibrio-susceptible bacteria in the three environments sampled is probably sufficient to support the growth of the bdellovibrios.

63. **Characterisation of 16 *Campylobacter jejuni* and *C. coli* typing bacteriophages. Sails, A. D., Wareing, D. R., Bolton, F. J., Fox, A. J., Curry, A. (1998). *Journal of Medical Microbiology* 47:123-128.** Taxonomic classification of bacteriophages specific for Campylobacter jejuni and C. coli has not been reported previously. A set of 16 virulent phages, distinguishable by their lytic spectra, has been used extensively for epidemiological typing of C. jejuni and C. coli at Preston Public Health Laboratory. These phages were investigated by electron microscopy, pulsed-field gel electrophoresis and restriction endonuclease analysis. All phages had icosahedral heads and long contractile tails. Accordingly, they were classified as members of the Myoviridae family. These phages could be subdivided into three groups according to genome size and head diameter: group I, two phages with head diameters of 140.6 and 143.8 nm and genome sizes of 320 kb; group II, five phages with average head diameters of 99 nm and average genome sizes of 184 kb; and group III, nine phages with average head sizes of 100 nm and average genome sizes of 138 kb. Phages NCTC12676 and NCTC12677 of group I had unusually large genomes of c. 320 kb which are two of the largest phage genomes to be described. Restriction endonuclease analysis demonstrated that DNA from the 16 phages was refractory to digestion by a number of restriction enzymes.

64. **Mycobacteriophages. Sarkis, G. J., Hatfull, G. F. (1999). *Methods in Molecular Biology* 101:145-173.**

65. **Molecular survey of the Salmonella phage typing system of Anderson. Schmieger, H. (1999). *Journal of Bacteriology* 181:1630-1635.** Typing phages for Salmonella and the prophages of their typical propagation strains were analyzed at the DNA level. Most of them belong to the P22 branch of the lambdoid phages. Acquisition of new plating properties of the typing phages by propagation in particular strains can be due to different host specific modifications of the DNA or to recombination events with residing prophages which are reflected by changes in the respective DNA restriction patterns. It is concluded that the actually available set of typing phages is a historically unique combination of strains.

66. ***Pseudomonas aeruginosa* phage lysate as an immunobiological agent. 1. Selection of *Pseudomonas aeruginosa* clinical strains for phage lysate preparation. Sekaninova, G., Kolarova, M., Pillich, J., Semenka, J., Slavikova, H., Kubickova, D., Zajicova, V. (1999). *Folia Microbiologica* 44:93-97.** A total of 2087 Pseudomonas aeruginosa isolates collected during the period 1994-1997 were used as starting material. Out of 1704 in-patient isolates, 299 strains were selected for the preparation of phage lysates but only five strains provided stable lysates, i.e., maintained the ability to be repeatedly and completely lysed by the appropriate phage in the course of several years. A set of 193 out-patients (189) and water sources (4) isolates failed to yield strains suitable for phage lysate preparation; 190 strains isolated abroad from patients with cystic fibrosis or respiratory infections included three isolates which, despite having a high degree of mucus production, were suitable for lysate preparation. The antigenic pattern of the phage lysates was ascertained by SDS-polyacrylamide gel electrophoresis.

67. **Sunlight inactivation of fecal bacteriophages and bacteria in sewage-polluted seawater. Sinton, L. W., Finlay, R. K., Lynch, P. A. (1999). *Applied and Environmental Microbiology* 65:3605-3613.** Sunlight inactivation rates of somatic coliphages, F-specific RNA bacteriophages (F-RNA phages), and fecal coliforms were compared in seven summer and three winter survival experiments. Experiments were conducted outdoors, using 300-liter 2% (vol/vol) sewage-seawater mixtures held in open-top chambers. Dark inactivation rates (k(D)s), measured from exponential survival curves in enclosed (control) chambers, were higher in summer (temperature range: 14 to 20 degrees C) than in winter (temperature range: 8 to 10 degrees C). Winter k(D)s were highest for fecal coliforms and lowest for F-RNA phages but were the same or similar for all three indicators in summer. Sunlight inactivation rates (k(S)), as a function of

cumulative global solar radiation (insolation), were all higher than the k(D)s with a consistent k(S) ranking (from greatest to least) as follows: fecal coliforms, F-RNA phages, and somatic coliphages. Phage inactivation was exponential, but bacterial curves typically exhibited a shoulder. Phages from raw sewage exhibited k(S)s similar to those from waste stabilization pond effluent, but raw sewage fecal coliforms were inactivated faster than pond effluent fecal coliforms. In an experiment which included F-DNA phages and Bacteroides fragilis phages, the k(S) ranking (from greatest to least) was as follows: fecal coliforms, F-RNA phages, B. fragilis phages, F-DNA phages, and somatic coliphages. In a 2-day experiment which included enterococci, the initial concentration ranking (from greatest to least: fecal coliforms, enterococci, F-RNA phages, and somatic coliphages) was reversed during sunlight exposure, with only the phages remaining detectable by the end of day 2. Inactivation rates under different optical filters decreased with the increase in spectral cutoff wavelength (50% light transmission) and indicated that F-RNA phages and fecal coliforms are more susceptible than somatic coliphages to longer solar wavelengths, which predominate in seawater. The consistently superior survival of somatic coliphages in our experiments suggests that they warrant further consideration as fecal, and possibly viral, indicators in marine waters.

68. **Images in Infectious Diseases in Obstetrics and Gynecology. Vaginal *Lactobacillus* phage plaques and electron micrograph. Tao, L., Pavlova, S. I. (1999). *Infectious Diseases in Obstetrics and Gynecology* 6:236-236.**

69. **Genome plasticity in the distal tail fiber locus of the T-even bacteriophage: recombination between conserved motifs swaps adhesin specificity. Tetart, F., Desplats, C., Krisch, H. M. (1998). *Journal of Molecular Biology* 282:543-556.** The adsorption specificity of the T-even phages is determined by the protein sequence near the tip of the long tail fibers. These adhesin sequences are highly variable in both their sequence and specificity for bacterial receptors. The tail fiber adhesin domains are located in different genes in closely related phages of the T-even type. In phage T4, the adhesin sequence is encoded by the C-terminal domain of the large tail fiber gene (gene 37), but in T2, the adhesin is a separate gene product (gene 38) that binds to the tip of T2 tail fibers. Analysis of phage T6 and Ac3 sequences reveals additional variant forms of this locus. The tail fiber host specificity determinants can be exchanged, although the different loci have only limited homology. Chimeric fibers can be created by crossovers either between small homologies within the structural part of the fiber gene or in conserved motifs of the adhesin domain. For example, the T2 adhesin determinants are flanked by G-rich DNA motifs and exchanges involving these sequences can replace the specificity determinants. These features of the distal tail fiber loci genetically link their different forms and can mediate acquisition of diverse host range determinants, including those that allow it to cross species boundaries and infect taxonomically distant hosts.

70. **Modeling the oddities of biology. Trivedi, B. (1998). *Nature Biotechnology* 16:1316-1317.**

71. **The clinically isolated FIZ15 bacteriophage causes lysogenic conversion in *Pseudomonas aeruginosa* PAO1. Vaca-Pacheco, S., Paniagua-Contreras, G. L., Garcia-Gonzalez, O., de la Garza, M. (1999). *Current Microbiology* 38:239-243.** FIZ15 bacteriophage, from a human clinical isolate of Pseudomonas aeruginosa, causes lysogenic conversion in the P. aeruginosa strain PAO1. The prophage-conferred phenotypes are: (1) increased resistance to phagocytosis by mouse peritoneal macrophages; (2) increased resistance to killing by normal human serum, and (3) increased adhesion to human buccal epithelial cells. These phenotypes are related to the prophage-induced change at the level of its own bacterial receptor, which appears to be the O-antigen.

72. **Isolation and characterization of APSE-1, a bacteriophage infecting the secondary endosymbiont of *Acyrthosiphon pisum*. van der Wilk, F. (1999). *Virology* 262:104-113.** A bacteriophage infecting the secondary endosymbiont of the pea aphid Acyrthosiphon pisum was isolated and characterized. The phage was tentatively named bacteriophage APSE-1, for bacteriophage 1 of the A. pisum secondary endosymbiont. The APSE-1 phage particles morphologically resembled those of species of the Podoviridae. The complete nucleotide sequence of the bacteriophage APSE-1 genome was elucidated, and its genomic organization was deduced. The genome consists of a circularly permuted and terminally redundant double-stranded DNA molecule of 36524 bp. Fifty-four open reading frames, putatively encoding proteins with molecular masses of more than 8 kDa, were distinguished. ORF24 was identified as the gene coding for the major head protein by N-terminal amino acid sequencing of the protein. Comparison of APSE-1 sequences with bacteriophage-derived sequences present in databases revealed the putative function of 24 products, including the lysis proteins, scaffolding protein, transfer proteins, and DNA polymerase. This is the first report of a phage infecting an endosymbiont of an arthropod.

73. **Characterization of the lysogenic bacteriophage MAV1 from Mycoplasma arthritidis. Voelker, L. L., Dybvig, K. (1998). *Journal of Bacteriology* 180:5928-5931.** The lysogenic bacteriophage MAV1, which is associated with the arthritogenicity of Mycoplasma arthritidis, was characterized. Several strains of M. arthritidis were examined for their ability to support growth of MAV1. A PFU assay was developed, and the sensitivity of phage to various chemical treatments was assayed. The most notable result was the resistance of MAV1 to proteinase K. The MAV1 genome is a double-stranded, linear DNA molecule of about 16 kb. The site of MAV1 DNA integration in the host chromosome was investigated. The ends of MAV1 DNA were cloned from three independent lysogens shown to have MAV1 DNA inserted at different sites in the host. The nucleotide sequences of the ends of the MAV1 genome and of the MAV1 DNA-chromosomal DNA junctions from each of three lysogens were determined. Sequences flanking the integrated prophage and the ends of native MAV1 DNA were determined, allowing the identification of the phage DNA (attP) and bacterial DNA (attB) recombination sites. Analysis of the left MAV1 DNA-chromosomal DNA junction sites showed a single-base heterogeneity located within MAV1 DNA sequences immediately adjacent to the attB sequence. A model for MAV1 integration-excision is proposed.

74. **Bacteriophage diversity in the North Sea. Wichels, A., Biel, S. S., Gelderblom, H. R., Brinkhoff, T., Muyzer, G., Schutt, C. (1998). *Applied and Environmental Microbiology* 64:4128-4133.** In recent years interest in bacteriophages in aquatic environments has increased. Electron microscopy studies have revealed high numbers of phage particles (10(4) to 10(7) particles per ml) in the marine environment. However, the ecological role of these bacteriophages is still unknown, and the role of the phages in the control of bacterioplankton by lysis and the potential for gene transfer are disputed. Even the basic questions of the genetic relationships of the phages and the diversity of phage-host systems in aquatic environments have not been answered. We investigated the diversity of 22 phage-host systems after 85 phages were collected at one station near a German island, Helgoland, located in the North Sea. The relationships among the phages were determined by electron microscopy, DNA-DNA hybridization, and host range studies. On the basis of morphology, 11 phages were assigned to the virus family Myoviridae, 7 phages were assigned to the family Siphoviridae, and 4 phages were assigned to the family Podoviridae. DNA-DNA hybridization confirmed that there was no DNA homology between phages belonging to different families. We found that the 22 marine bacteriophages belonged to 13 different species. The host bacteria were differentiated by morphological and physiological tests and by 16S ribosomal DNA sequencing. All of the bacteria were gram negative, facultatively anaerobic, motile, and coccoid. The 16S rRNA sequences of the bacteria exhibited high levels of similarity (98 to 99%) with the sequences of organisms belonging to the genus Pseudoalteromonas, which belongs to the gamma subdivision of the class Proteobacteria.

75. **Biodistribution of filamentous phage-Fab in nude mice. Yip, Y. L., Hawkins, N. J., Smith, G., Ward, R. L. (1999). *Journal of Immunological Methods* 226:171-178.** In vivo panning of peptide libraries in mice has allowed the isolation of peptides which target the vasculature of specific organs. The application of this approach to phage displaying Fab fragments (phage-Fab) could lead to the isolation of antibodies which recognize novel tumor antigens. In this study, we have evaluated the biodistribution of phage-Fab in nude mice. Balb/c nude mice were injected intravenously with 10(9) TU of phage displaying the anti-colon cancer Fab c30.6. Blood samples were collected at nine time points over a period of 72 h and three groups of four mice were sacrificed at 4 min, 24 h and 72 h. Normal tissues (liver, colon, spleen, kidneys, lungs, skeletal muscle) and faeces were collected at these time points and the number of viable phage in each sample was determined. The distribution of phage in tissues was also examined by immunohistochemical analysis of paraffin-embedded tissues. Regression analysis of plasma kinetic data showed that the half-life and the volume of distribution of phage was 3.6 h and 1 ml, respectively. Phage uptake occurred predominantly in lungs, kidneys, spleen and liver. Relatively few phage were distributed to colon and muscle, and phage were eliminated from the circulation by

72 h. Immunohistochemical analysis showed phage to be mainly within the vasculature at 4 min, whereas notable phage extravasation was observed at 24 h and 72 h. In conclusion, this study provides information on the in vivo behavior of phage-Fab which will be useful in the design of in vivo panning strategies. By choosing appropriate time points for tissue collection, it may be possible to isolate novel Fabs against both intra- and extravascular targets.

76. **Amplification and spread of viruses in a growing plaque. You, L. (1999).** ***Journal of Theoretical Biology*** **200:365-373.** The two-dimensional propagation of viruses through a "lawn" of receptive hosts, commonly called plaque growth, reflects the dynamics of interactions between viruses and host cells. Here we treat the amplification of viruses during plaque growth as a reaction-diffusion system, where interactions among the virus, uninfected host cells, and virus-producing host-virus complexes are accounted for using rates of viral adsorption to and desorption from the host-cell surface, rates of reproduction and release of progeny viruses by lysis of the host, and by the coupling of these reactions with diffusion of free virus within the agar support. Numerical solution of the system shows the development of a traveling wave of reproducing viruses, where the velocity of the wave is governed by the kinetic and diffusion parameters. The model has been applied to predict the propagation velocity of a bacteriophage plaque. Different mechanisms may account for the dependence of this velocity on the host density during early stages of a growing plaque. The model provides a means to explore how changes in the virus-host interactions may be manifest in a growing plaque.

77. **Svoistva mikobakteriofaga MTPN11 [Properties of MTPN11 mycobacteriophage]. Zhilenkov, E. L., Shemakin, I. G., Stepanshina, V. N., Korobova, O. V., Oborotov, M. V., Dorozhkova, I. R. (1998).** ***Mikrobiologica*** **67:660-665.** Some characteristics of the poorly studied phage MTPH11, which is used for identification of mycobacteria, are presented. The phage has an isometric head and a long noncontractile tail (B1 morphotype). The attachment apparatus of this phage includes a basal plate composed of two joint disks and a single tail fiber. The constant of phage adsorption on Mycobacterium smegmatis ATCC607 cells is 6.6 x 10(-9) ml/min. The latent infection period in the MTPH11-host strain 607 system in 65 min; phage progeny ranges from 30 to 40 virions per one cell. The constant of phage inactivation with a homologous antiserum is 50 min-1. The buoyant density of intact MTPH11 virion in CsCl amounts to 1.520 g/cm3. The phage is susceptible to chloroform, retains lytic activity within a pH range of 5 to 9, and is resistant to inactivating agents. The G + C content of the phage DNA is 63 mol%.

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Acknowledgements

Thank you to Hans Ackermann for this quarter's submission.

Contact Steve Abedon (microdude+@osu.edu) with suggestions, criticisms, comments, or anything else that might help make this a better site.