



## Multicellular defense against phage infection in *Streptomyces* – impact of secondary metabolites and mycelial development

Larissa Kever

Schlüsseltechnologien / Key Technologies

Band / Volume 274

ISBN 978-3-95806-724-0

Forschungszentrum Jülich GmbH  
Institut für Bio- und Geowissenschaften  
Biotechnologie (IBG-1)

# **Multicellular defense against phage infection in *Streptomyces* – impact of secondary metabolites and mycelial development**

Larissa Kever

Schriften des Forschungszentrums Jülich  
Reihe Schlüsseltechnologien / Key Technologies

Band / Volume 274

---

ISSN 1866-1807

ISBN 978-3-95806-724-0

## Table of contents

1. Summary.....	1
2. Scientific context and key results.....	3
2.1. Bacteriophages: Ubiquitous bacterial viruses shaping bacterial evolution .....	3
2.1.1. Discovery, classification and life style.....	3
2.1.2. (Pro-)phage proteins affecting bacterial hosts.....	6
2.1.3. Bacterial antiphage defense systems .....	8
2.2. <i>Streptomyces</i> , a filamentous soil bacterium as major producer of bioactive compounds	12
2.2.1. Multicellular development and its hierarchical regulatory network .....	12
2.2.2. Complex secondary metabolism as hallmark of <i>Streptomyces</i> .....	14
2.3. Multicellular antiphage defense systems of <i>Streptomyces</i> .....	17
2.3.1. Phage infection of <i>Streptomyces</i> : Initial observations .....	17
2.3.2. Chemical defense via aminoglycoside antibiotics .....	19
2.3.3. Inactivation of infectious phage particles in the extracellular space.....	28
2.3.4. Community-wide protection against phage infection .....	37
2.4. Conclusion and perspectives .....	41
2.5. References.....	43
3. Publications and manuscripts .....	59
3.1. Identification of Gip as a novel phage-encoded gyrase inhibitor protein of <i>Corynebacterium glutamicum</i> .....	60
3.2. Aminoglycoside antibiotics inhibit phage infection by blocking an early step of the infection cycle.....	74
3.3. Inactivation of phage particles in the extracellular space of <i>Streptomyces</i> populations ..	91
3.4. Genome sequence and characterization of five bacteriophages infecting <i>Streptomyces coelicolor</i> and <i>Streptomyces venezuelae</i> : Alderaan, Coruscant, Dagobah, Endor1 and Endor2 .....	108
3.5. Antiphage small molecules produced by bacteria – beyond protein-mediated defenses .....	124

4. Appendix.....	140
4.1. Appendix to 3.1. Identification of Gip as a novel phage-encoded gyrase inhibitor protein of <i>Corynebacterium glutamicum</i> .....	140
4.2. Appendix to 3.2: Aminoglycoside antibiotics inhibit phage infection by blocking an early step of the infection cycle.....	202
4.3. Appendix to 3.3: Inactivation of phage particles in the extracellular space of <i>Streptomyces</i> populations.....	227
4.4. Appendix to 3.4: Genome sequence and characterization of five bacteriophages infecting <i>Streptomyces coelicolor</i> and <i>Streptomyces venezuelae</i> : Alderaan, Coruscant, Dagobah, Endor1 and Endor2 .....	239
 Acknowledgements .....	 243
 Erklärung .....	 245

Schlüsseltechnologien / Key Technologies  
Band / Volume 274  
ISBN 978-3-95806-724-0