

Signalling pathways that control development and antibiotic production in streptomyces

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STELLINGEN behorende bij het proefschrift

Propositions accompanying the thesis

SIGNALLING PATHWAYS THAT CONTROL DEVELOPMENT AND ANTIBIOTIC PRODUCTION IN STREPTOMYCES

- 1. The discovery of sugar isomerase SCO4393 shows that, even after decades of intensive study, new key enzymes in central metabolism can still be discovered (this thesis, Chapter IV).
- 2. *Aminosugar sensitivity* describes the inability of mutants lacking certain metabolic enzymes to grow on the substrate; given that the existence of this phenomenon has been known for almost 50 years, it may be unlikely that we will soon discover its cause (this thesis, Chapter VII; Bernheim & Dobrogosz, 1970; Kadner *et al.*, 1992).
- 3. Mutants lacking a functional NagA enzyme, which consequently accumulate high levels of GlcNAc-6P, are sensitive to GlcNAc in *Escherichia coli* and *Bacillus subtilis* but not in *Streptomyces coelicolor*. This suggests major differences in aminosugar metabolism, processing and/or connecting pathways (this thesis; Świątek et al., 2012a; Plumbridge, 2015).
- 4. The ability of *nagK* disruptions to relieve the toxicity of GlcNAc in *Streptomyces coelicolor nagB* mutants raises new questions about the metabolism of GlcNAc under conditions presumed to involve PTS transport and the status of the intracellular GlcNAc pool (this thesis, Chapter V).
- 5. Studying the metabolism of 2-deoxy-glucose in *Streptomyces* may provide new clues for the as yet unexplained mode of action of this anticancer drug (this thesis, Chapters VI; Ralser et al., 2008).
- 6. The dormancy regulator OsdR controls a remarkably brief but major change in the global transcription profile of *Streptomyces coelicolor* during the onset of development on minimal media (this thesis, Chapter III).
- 7. It is probably not a coincidence that many of the stress-related genes controlled by OsdR lie in close proximity to *osdRK* on the genome (this thesis, Chapter III).

- 8. The recognition sequences of some ROK-family proteins are highly conserved and, as such, researchers must carefully examine the subtle but important differences between these regulators (this thesis, Chapter VI; Brechemier-Baey *et al.*, 2015).
- 9. Unpublishable data, including so-called 'negative results', are useful and relevant to the scientific community and, as such, also require a forum for data-sharing.
- 10. The pen is mightier than the sword, but the pipette is mightier still (adapted from Edward Bulwer-Lytton).