New Insights in *Streptomyces* Fermentations

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*Streptomyces* is a very important industrial bacterium, which produces two thirds of clinically relevant secondary metabolites. It is considered as a “multicellular” prokaryotic model that includes programmed cell death (PCD) and sporulation in solid cultures. *Streptomyces* industrial fermentations are mainly produced in liquid cultures (large bioreactors) conditions in which most species do not sporulate, and it was traditionally considered that there was no differentiation. It has been almost unanimously accepted that mycelial morphology in liquid fermentation was correlated with the production of secondary metabolites, albeit the cause-effect relationship was controversial: some authors hold that cellular aggregation, and hence pellet and clump formation is fundamental to obtaining good production of secondary metabolites. On the other hand, other authors state that there is no relationship between morphology and secondary metabolite production. In conclusion, there was no general consensus correlating morphology with secondary metabolite production, and the lack of a consistent developmental model in *Streptomyces* hindered the precise description of reliable phenotypes to analyse and optimize industrial fermentations.

New drugs, especially antibiotics, are urgently required in clinic and the most propitious natural source remained in environmental bacteria, especially *Streptomyces*. The screening for new secondary metabolites was traditionally performed by means of strain isolations, cultures and bioassays [1], a process tremendously productive during the “Golden Age” of antibiotics (1940s–1960s), but which was becoming more and more difficult once the most common antibiotics were already discovered. The main handicap of this screening approach was the high number of false negatives: i.e. strains discarded as bioactive compound producers, because they did not reach the producing phase in the screening process. These strains are indicated. Their development was critiqued to design new experimental approaches to optimize the selection process and to avoid the large number of false negatives. The new *Streptomyces* developmental cycle opens a new background in which study differentiation, and it will be the key for the analysis and optimization of *Streptomyces* development.

**Figure 1:** *Streptomyces* developmental cycle in solid (sporulating) and liquid (non-sporulating) cultures. MI, first compartmentalized mycelium, mycocyte. MII, second multinucleated mycelium, antibiotic producer. The classical nomenclature of substrate and aerial mycelium, and the hydrophobic layers are indicated.

**References**


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