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► To cite this version:

Aaron Millan Oropeza, Celine Henry, Clara Lejeune, Michelle David, Marie-Jöelle Virolle. Quantitative proteomics revealed the nature and cause of the different metabolic features underpinning weak and strong antibiotic producing abilities of two model *Streptomyces* species. SFEAP 2019, Société Française d'Electrophorèse et d'Analyse Protéomique (SFEAP). FRA., Sep 2019, Strasbourg, France. pp.1. hal-02342396

HAL Id: hal-02342396

<https://hal.science/hal-02342396>

Submitted on 5 Jun 2020

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Quantitative proteomics revealed the nature and cause of the different metabolic features underpinning weak and strong antibiotic producing abilities of two model *Streptomyces* species

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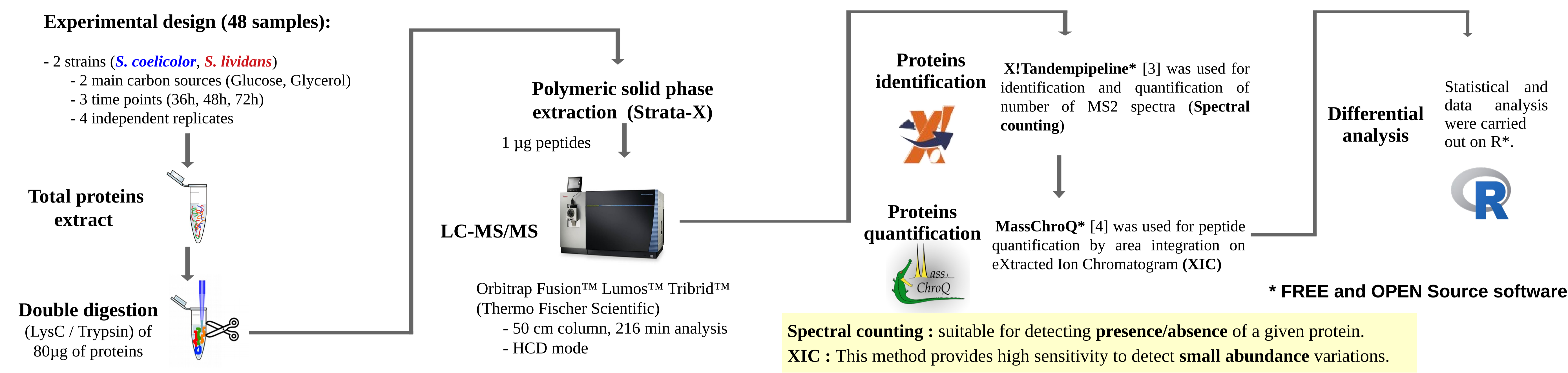
CONTEXT OF STUDY

The *Streptomyces* genus is well known for its ability to produce numerous and diverse bio-active molecules useful to human health. The biosynthesis of these specialized metabolites usually occurs when growth slows down or stops and is triggered by nutritional limitations, especially by phosphate.

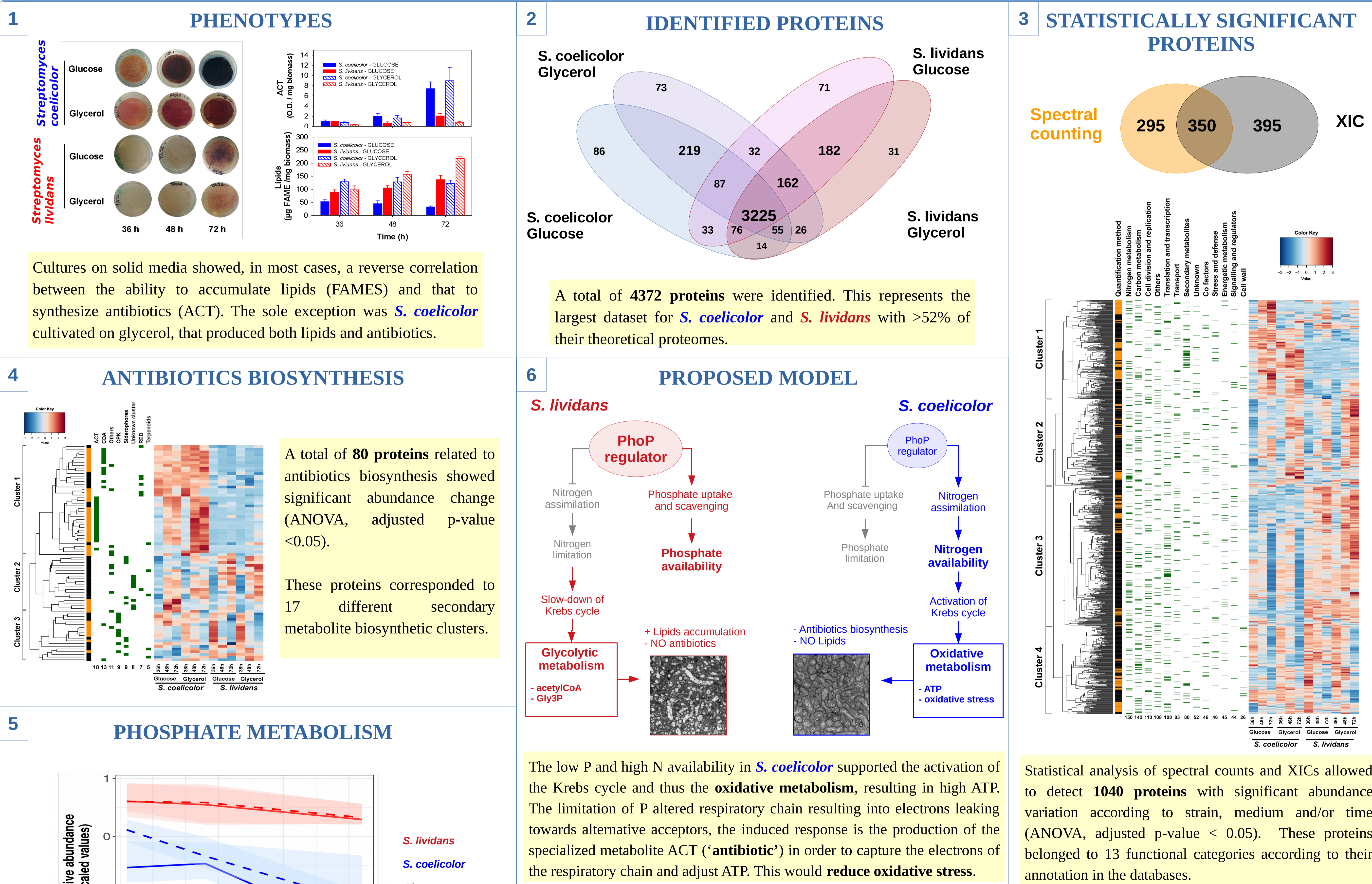
Two model species commonly used to understand the biosynthesis of these bio-active metabolites are *S. coelicolor* M145 and *S. lividans* TK24. These species are closely related (95% of orthologous genes) but exert different abilities to produce three well characterized secondary metabolites (CDA, RED, ACT). In presence of glucose as main carbon source, the **high antibiotic** production of *S. coelicolor* was correlated with a **low lipid** content whereas *S. lividans* showed a poor ability to synthesize antibiotics that was correlated with higher lipid content [1].

Despite numerous important scientific contributions over the past 40 years, a systemic understanding of the biosynthesis of these bio-active metabolites and the metabolic feature characterizing the producing bacteria remains incomplete. To progress on the field, a label-free shotgun comparative proteomic analysis was carried out in *S. coelicolor* M145 and *S. lividans* TK24 cultivated under different carbon sources and studied at different times of culture [2].

METHODOLOGY



RESULTS



CONCLUSION

* This work is pioneering in the elucidation of the basis of the metabolic differences underlying the drastically different abilities of *S. coelicolor* and *S. lividans* to produce antibiotics.

* The low abundance of the TCS PhoR/PhoP in *S. coelicolor* compared to *S. lividans* led to an alleviation of its regulatory role likely to be responsible of the specific metabolic features of this strain (see model).

* A novel view of the role of the antibiotics in the physiology of the producing bacteria was proposed. These molecules would play an important role in the regulation of the energetic metabolism of the bacteria in condition of phosphate scarcity.

[1] Le Marechal P, Decottignies P, Marchand CH, Degrouard J, Jaillard D, Dulermo T, Froissard M, Smirnov A, Chapuis V, Virolle M. (2013). Comparative proteomic analysis of *Streptomyces lividans* wild-type and ppk mutant strains reveals the importance of storage lipids for antibiotic biosynthesis. *Appl Environ Microbiol*, 79(19): 5907-17.

[2] Millán-Oropeza A. (2017). Comparative study of the proteome of *S. coelicolor* M145 and *S. lividans* TK24, two phylogenetically closely related strains with very different abilities to accumulate TAG and produce antibiotics. Université Paris-Saclay. NNT : 2017SACL15160.

[3] Langella O, Valot B, Balliau T, Blein-Nicolas M, Bonhomme L, Zivy M. (2017). X!TandemPipeline: a tool to manage sequence redundancy for protein inference and phosphosite identification. *J Proteome Res*. 16(2): 494-503.

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