

Syntheroids: Synthetic Biology for Industrial Production of Steroids

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Steroids are the second largest class of drugs for medical applications, only exceeded by antibiotics. Currently, there are more than 300 clinically approved steroidal compounds, representing a 10 billion USD market. Although the production of key steroid intermediates (mainly C19-steroids) from phytosterols has been industrialized, there is still considerable room for improvement and many challenges remain. The generation of effective engineered production strains, improved bioprocess efficiency, improved product recovery, and the problem of end-product inhibition, are major challenges for the industry. The **Syntheroids** project aims to develop integrative processes for innovative bioconversion of phytosterols to C22-steroids based on Synthetic Biology of non-pathogenic Actinobacteria (*Mycobacterium*, *Nocardioides*). These compounds are key intermediates in the synthesis of several therapeutic steroids applied in gastroenterology and endocrinology.

Steroid pharmaceuticals are important for life quality, healthy development and ageing, all major challenges today. Production of key intermediates for the synthesis of therapeutic steroids, in an eco-friendly and economical process, is the main expected result of **Syntheroids**. Today, a handful of steroid precursors are industrially produced from phytosterols, mostly by companies in China, India and the US, but some companies are also located in Europe. All in fierce and keen competition. Innovative ideas that can expand the list of steroids produced from phytosterols in a single-step biotechnological process are wanted, and this is why

two European companies (Bionice and Pharmins Ltd.) are active partners in the five-partner Consortium **Syntheroids**. Shorter steroid production pipelines and eco-friendly processes, in compliance with European regulations, will increase the EU-GDP (gross domestic product), increase the companies' competitiveness, and reduce the medical costs for the drug users.

Objectives

The main objective of **Syntheroids** is to develop an integrated production process for pharmaceutical steroids using Synthetic Biology and improved processing technology.

To achieve this goal, the **Syntheroids** project has the following four specific objectives:

- Omics data integration from steroid producing Actinobacteria as a source of Synthetic Biology targets for production strain evolution.
- Creating genetically engineered bacterial strains capable of producing innovative C22 steroid precursors.
- Reduce or eliminate end-product inhibition by mutagenesis, genetic engineering and process optimization.
- Integrate up- and downstream processes for an eco-friendly bioconversion.