Inhibitors of ribosome assembly

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Pharma

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Track 1

SUMMARY

In this project it is planned to develop a new class of antibiotics, based on the inhibition of prokaryotic ribosome assembly. According to the WHO antibiotic resistance is a global threat. The team has developed an *in-vivo* screening assay based on reporter strains, where large and small ribosomal subunits have been tagged with red or green fluorescent proteins. A disturbance in subunit assembly can be detected via the fluorescent ratio. Based on this fluorescence-based reporter assay, a high throughput screen was performed to identify small molecule inhibitors that specifically interfere with the assembly of either the large or the small ribosomal subunit and thereby inhibit bacterial growth.

PROJECT ACHIEVEMENTS DURING & AFTER SPARK

- HTS was performed at the FMP
- Due to low specificity of the screening assay hit candidates could not be identified
- Advise to improve the screening assay & evaluate alternative approaches (e.g. structure-based design)
- Identified hit compounds in in-silico structure-based design methods in collaboration with AG-Wolber (FU Berlin)
- Hit compounds are being tested in several assays.