

## Title

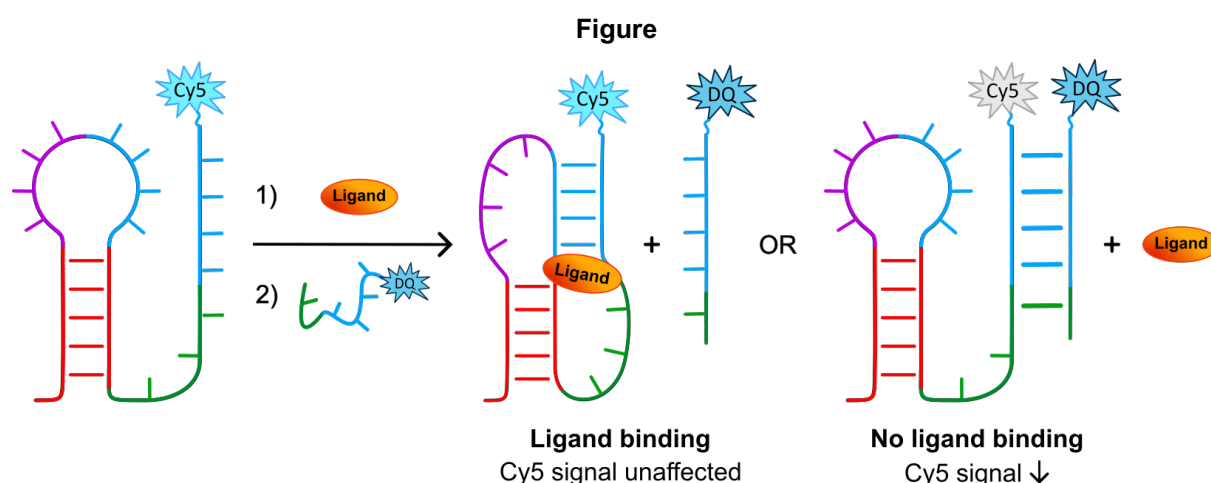
High throughput screening assay for targeting tertiary RNA structures

## Authors

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### Poster presentation

The SARS-CoV-2 pandemic and ever-growing antibiotic-resistance have highlighted the importance of the development of new antimicrobials. Recently, a field in drug development has emerged that focusses on targeting RNA instead of proteins to treat disease, in hopes of finding medicine for currently untreatable diseases. In this research, two complex RNA structures called the RNA pseudoknot and the RNA G-quadruplex are targeted, which are used by some bacteria and viruses to regulate gene expression. In my research, I am looking for novel ligands for three promising antimicrobial targets: the bacterial PreQ<sub>1</sub>-riboswitch<sup>1</sup>, the SARS-CoV-2 frameshifting pseudoknot and a SARS-CoV-2 G-quadruplex. Since measuring small-molecule-RNA interactions is challenging, I have developed an innovative competitive antisense binding assay that can detect small molecule-RNA binding in a high throughput fashion. With this method, I have screened an RNA-focussed small-molecule library comprising 15,520 compounds, from which several interesting hits emerged. These hits will be further validated in various *in vitro* and *in cellulo* biological assays (gene regulation- and frameshifting assays, MICs, etc.) and optimized in a medicinal chemistry program, in hopes of developing a new generation of antimicrobials.



### References (max 3)

- (1) Wintermans, S. E. L.; Hoffmann, J. S.; Tacoma, M. D.; Broekhuizen, I.; Doodewaerd, B. R. van; Geurink, P. P.; Janssen, A. P. A.; Artola, M.; Olsthoorn, R. R. C. L. High-Throughput Competitive Binding Assay for Targeting RNA with Small Molecules: Discovery of New PreQ<sub>1</sub> Riboswitch Ligands. *bioRxiv* May 22, 2024, p 2024.05.22.595132. <https://doi.org/10.1101/2024.05.22.595132>.