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Live cell assay to quantify the activity of SARS-CoV-2 main protease, Mpro

Fluorescence-based method to effectively screen for protease inhibitors

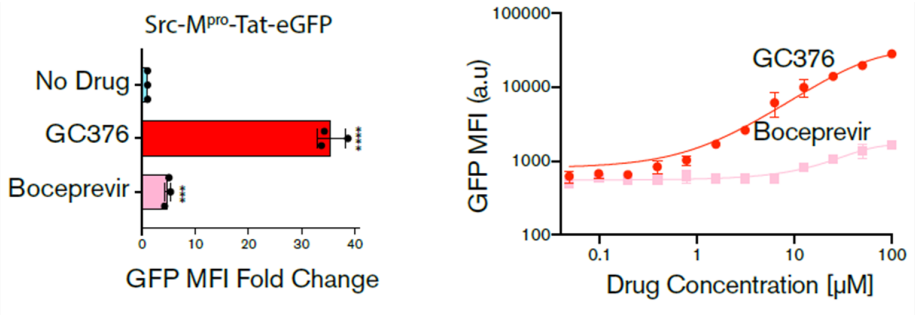

Fig. 1. GC376 is more potent than boceprevir in blocking SARS-CoV-2 M^{pro} function in 293T cells. Moghadasi, S. et al., 2020. bioRxiv.

Technology ID

2021-102

Category

Life Sciences/Human Health
Life Sciences/Pharmaceuticals
Life Sciences/Therapeutics

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IP Status: US Patent Pending

Applications

- Screening, characterization, and development of protease inhibitors against SARS-CoV-2 and related coronaviruses

Key Benefits & Differentiators

- **Robust quantification system:** live cell, fluorescence-based gain-of-function assay for inhibitor screening
- **High specificity and sensitivity:** exquisite specificity and high signal-to-noise ratio

Technology Summary

Despite the ongoing COVID-19 pandemic, there are still no effective drugs to treat disease caused by SARS-CoV-2. SARS-CoV-2 viral proteases (M^{pro} or PL^{pro}) and the RNA dependent RNA polymerase (RdRp) are ideal targets for drug discovery. The main protease, M^{pro}, is required to cleave the viral polyprotein into precise functional units for virus replication and pathogenesis and is therefore an attractive drug target. A wide range of biochemical assays are available for measuring SARS-CoV-2 protease activity, but specific and sensitive cellular assays are less developed. There are currently no sensitive and specific live cell assays available for quantifying SARS-CoV-2 M^{pro} inhibition, which hinders development of drugs to target this enzyme.

Researchers at the University of Minnesota have developed a quantitative reporter for M^{pro} function in living cells (Src-Mpro-Tat-eGFP), in which protease inhibition by genetic or chemical methods results in strong eGFP fluorescence (**Fig. 1**). This robust gain-of-function system readily distinguishes between inhibitor potencies and can be scaled-up to high-throughput platforms for drug development. Essentially, the better the chemical inhibitor/drug, the stronger the

fluorescent readout of the assay which expedites any high-throughput readout.

Phase of Development

TRL: 4-6

Proof of concept with commercial inhibitors and tested in 293, 293T, HeLa and U2OS cell lines.

Desired Partnerships

This technology is now available for:

- License
- Sponsored research
- Co-development

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Researchers

- **Reuben S. Harris, PhD** Professor, Biochemistry, Molecular Biology, and Biophysics Department

References

1. Moghadasi, S.A., Becker, J.T., Belica, C., Wick, C., Brown, W.L. and Harris, R.S.(2020) , Gain-of-function assay for SARS-CoV-2 Mpro inhibition in living cells, https://doi.org/10.1101/2020.11.09.375139