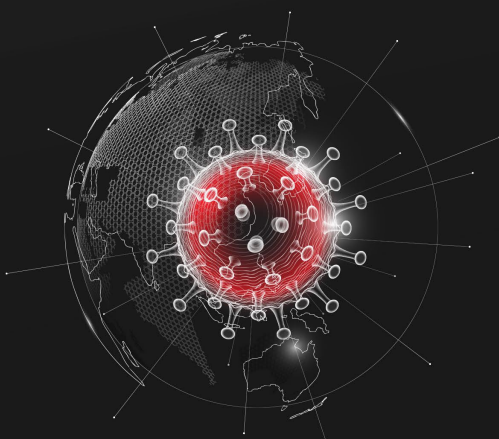


Genetically Encoded BRET-Based SARS-CoV-2 Mpro Protease Activity Sensor

GREAT NEED FOR COVID-19 TREATMENTS

COVID-19 is a global health threat with more than 238 million infections and nearly 5 million deaths as of October 2021.



VALIDATES THERAPEUTIC EFFECTIVENESS

Addressing the need to develop SARS CoV-2 therapeutics and diagnostics, researchers at HBKU have created a bioluminescence-based assay that detects activity of the chymotrypsin like protease or the main protease in SARS-CoV-2 replication.

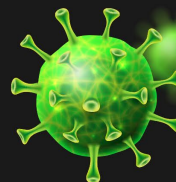
Mpro plays a critical role in virus replication, and monitoring its activity in a cell creates a reliable method of screening potential SARS-CoV-2 therapeutics. The technology is an engineered pair of genetically encoded, bioluminescence resonance energy transfer (BRET)-based sensors.

These sensors enable identification of proteolytic activity of Mpro in living host cells. Co-expression of the sensor with the Mpro in live cells results in its cleavage in a dosedependent manner, while mutation of the critical C145 residue (C145A) in Mpro completely abrogates the sensor cleavage-dependent signal decrease.

APPLICATIONS

These sensors find direct utility in:

- Validating the effectiveness of candidate therapeutics for COVID-19
- Detecting active SARS CoV-2 infections
- Determining effects of genetic variation in the Mpro amino acid sequence that may arise during the evolution of the virus



VALUE PROPOSITIONS

Mpro, essential for viral replication, is a key target for anti-SARS-CoV-2 agents. This technology uses a BRET pair (NLuc and mNG) flanking Mpro's autocatalytic peptide sequence for reliable live-cell and in vitro assays.

High sensitivity: BRET, using NLuc as the donor and mNG as the acceptor, allows highly sensitive detection of Mpro activity in live cells and in vitro.

High specificity: Sensors show no cleavage without Mpro or with the catalytically inactive C145A mutant.

Robust cleavage activity: Sensor constructs exhibit robust, dose- and time-dependent cleavage activity with wild-type Mpro in live cells and in vitro.

Wide dynamic range: Short and long sensor expressing cells showed a 75% BRET ratio reduction with wild-type Mpro, demonstrating a broad dynamic range for monitoring Mpro activity in live cells.



PATENT STATUS

Patent US 20240240228A1 has published



LICENSING OPPORTUNITIES

Hamad Bin Khalifa University is offering this technology for license. For more information, please contact: innovation@hbku.edu.qa