Technology Offer CSIC/AH/042

New antiviral familiy of compounds targeting of non-essential viral proteins

Novel antiviral strategy targeting viral non-essential proteins (NEPs), scarcely prone to adaptive mutations. As a proof of concept, SARS-CoV-2 ORF9b homodimerization inhibitors have been identified that prevents the virus hyperinflammation response.

Intellectual Property

EP patent application filled

Stage of development

Preclinical development

Intended Collaboration

Licensing and/or co-development

Contact

Ana Sanz

Vice-presidency for Innovation and Transfer

ana.sanz@csic.es
comercializacion@csic.es

Market need

Current antivirals become ineffective over time, largely owed to the accrual of adaptive and escape mutations in target viral proteins. As a novel antiviral strategy, scientists have built a discovery pipeline targeting viral non-essential proteins (NEPs), scarcely prone to adaptive mutations.

CSIC solution

As a proof of concept, they have targeted the SARS-CoV-2 NEP (accessory protein) ORF9b and its homodimerization, by applying structure-guided design approaches, chemical synthesis and optimization, experimental protein-protein interaction assays, and in vitro functional assays.

First-in-class inhibitors of ORF9b homodimerization have been identified that counter the pro-inflammatory activities and interferon anergy induced by ORF9b at low micromolar concentrations. The inhibitors have shown to prevent ORF9b mitochondrial localization and activation of inflammasome mediated caspase-1. Moreover, compounds restore IFN-1 responses compromised by viral ORF9b.

Competitive advantages

- Novel antiviral strategy have been identified targeting viral non-essential proteins, which are less susceptible to adaptive mutations.
- Based on structural analysis, SARS-CoV-2 ORF9b inhibitors should be active in all coronaviruses, including SARS-CoV and MERS.
- Same approach is being used to target other viral NEP of interest in human or animal pathology, such as the influenza A protein NS-1.