



PhD Research Proposal Form China Scholarship Council (CSC) - ENS Group

FIELD: Life sciences

Thesis subject title: **Translational control of viruses by the innate defense factor ISG20 (interferon-sensitive gene 20)**

Name of the French doctoral school : Integrative cellular and molecular biology (BMIC)

Name of the Research team : Laboratory of Primate Lentiviruses Lyon (LP2L)

Website : <https://ciri.ens-lyon.fr/teams/lp2l>

Name of the Supervisor : Andrea CIMARELLI

Email : acimarel@ens-lyon.fr

Lab Language : English

Research Proposal Abstract :

The molecular identification and characterization of innate defense factors that modulate viral replication is a key challenge in infectious diseases at the frontier between basic comprehension of the infection process and its translation to the clinical practice. In this category, the interferon-sensitive gene 20 (ISG20) is a member of the DnaQ-like 3'-5' exonuclease superfamily (or DEDD, for Asp-Glu-Asp-Asp) that has been associated to broad viral inhibition (VSV, Dengue, HIV etc). Using VSV as model for highly replicative RNA viruses in a study recently published on Plos Pathogens, we have demonstrated that ISG20 affects viral replication by inhibiting the translation of viral RNAs in the absence of their degradation. More importantly, we have demonstrated that this mechanism of translational control could distinguish RNAs of cellular origins, that are not affected, from viral ones that are instead inhibited. Through different approaches in cell biology, biochemistry and virology this PhD proposal aims at understanding how ISG20 can distinguish self, from non-self RNAs and act as a sentinel of cellular translation against a broad range of viruses. This could pave the way for the development of novel general antiviral treatments effective against several different viruses. The candidate will be directly tutored by the head of the lab and will be formed to the latest techniques in cell imaging, virus tracing and more generally in virology.

References : 1. Wu. The interferon stimulated gene 20 protein (ISG20) is an innate defense antiviral factor that discriminates self versus non-self translation. *PLoS Pathog* 2019. 2. Zhong. A novel domain within the CIL regulates egress of IFITM3 from the Golgi and reveals a regulatory role of IFITM3 on the secretory pathway. *Life Science Alliance* 2022. 3. Song. Trim69 is a microtubule regulator that acts as a pantropic viral inhibitor. *PNAS* 2022. 4. Deymier. Interferon-stimulated gene 20 kDa protein (ISG20), an enigmatic antiviral RNase targeting multiple viruses. *Febs Open Bio* 2022 5. Tartour. Interference with the production of infectious viral particles and bimodal inhibition of replication are broadly conserved antiviral properties of IFITMs *PLoS Pathog* 2017.

Type of PhD :

1. Full PhD

- Joint PhD/cotutelle (leading to a double diploma) : NO
- Regular PhD (leading to a single French diploma) : YES

2. Visiting PhD (for students enrolled at a Chinese institution who will be invited to a French institution to carry out a mobility period) : NO

--