N°23

Genomic surveillance and impact of SARS-CoV-2 mutations

Paula Ruiz-Rodriguez[1]; Miguel Álvarez-Herrera[1]; Maria Luisa Franco[2]; Clara Francés-Gómez[1]; María Carmen Marques[1]; Julia Hillung[1]; Eugenia Ulzurun[3]; Francisco José Martínez-Martínez[2]; Simón Rodríguez Santana[4]; Roi Naveiro Flores[4]; Daniel García Rasines[4]; Alberto Marina[2]; Jose Luís Llácer[2]; Marçal Vidal[2]; Sorzano Carlos Óscar S. [5]; Nuria E. Campillo[3]; Vicente Rubio[2]; Jose Maria Carazo[5]; Carmen Gil[3]; David Ríos[4]; Fernando González- Candelas[6]; Ron Geller[1]; Iñaki Comas[2]; Santiago F. Elena[1]; **Mireia Coscolla[1]**

Background. Deciphering the impact of SARS-CoV-2 mutations in immune evasion is essential to understand the dynamics of the epidemic. We aim to better understand the potential of different SARS-CoV-2 variants for impacting transmissibility and virulence.

Methods. We employ a complex workflow starting with mutation detection and epidemiological investigation, to further characterise the impact of mutations in the structure of the SARS-CoV-2 proteins and in the biology of a pseudovirus system in vitro (Figure 1). Mutation surveillance has employed different datasets including a global dataset with more than seven million viral sequences, and three local datasets up to ten thousand sequences paired with detailed hospitalisation and vaccination host information.

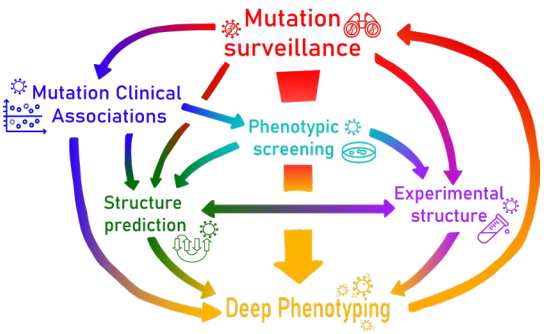
Results. First we have identified cluster 1163.7, characterised by spike mutations S:D1163Y and S:G1167V inside cluster 20E and we concluded that the two spike mutations impacted syncytia formation and infectivity in vitro. However, they did not impact thermal stability or neutralisation by antibodies except from those infected in the first Spanish epidemic wave.

Second, we have studied which combinations of S1 terminal domain spike mutations present in two variants of concern are more transmissible in different epidemiological settings.

Third, we have studied the diversity and migration dynamics of variants of concern.

Finally, we have used different statistical approaches to find associations between viral genomic variants and breakthrough infections and/or hospitalisation.

Conclusions. We have characterised SARS-CoV-2 variants circulating globally, with special focus in Spain, and studied the association of specific viral variants with vaccine breakthrough, hospitalisation, and transmission. Our study provides an effective pipeline for the characterization of biological fitness driven by the early identification of mutations of relevance in SARS-CoV-2, and followed by in vitro viral characterization and protein structure elucidation.



GRAPHICAL ABSTRACT

1 Instituto de Biología Integrativa de Sistemas, Universidad de València, (I2SysBio-CSIC-UV)

2 Instituto de Biomedicina de Valencia (IBV-CSIC)

3 Centro de Investigaciones Biológicas Margarita Salas (CIB-CSIC)

4 Instituto de Ciencias Matemáticas (ICMAT-CSIC)

5 Centro Nacional de Biotecnología (CNB-CSIC)

6 Instituto de Biología Integrativa de Sistemas, Universitat de València (I2SysBio-UV-CSIC)