Analysis of SARS-CoV-2 Spike Protein Mutations with Logistic Regression

Simón Rodríguez Santana, Roi Naveiro, Daniel García Rasines, Paula Ruiz-Rodriguez, Miguel Álvarez-Herrera, David Ríos Insua, Nuria E. Campillo, Eugenia Ulzurrun, Mireia Coscollá

ICMAT Datalab

About us…

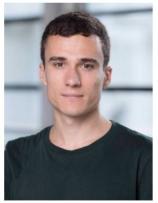
- **ICMAT** - Severo Ochoa Excellence Award (3 times)
- **Datalab group** (https://www.datalab.icmat.es) AXA-ICMAT Chair since 2014
- Framework projects since 2014

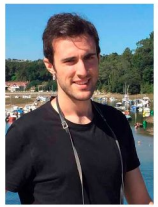

David Ríos


Nuria Campillo


Roi Naveiro


César Guevara


Daniel García


Simón Rodríguez

- Collaboration with **I2SysBio**, **CBM** & **CIB Margarita Salas** **(PTI Salud Global)**

Objective

Which mutations (individually or by pairs) of the COVID-19 genome are associated to important aspects of the infection?

- Severity - **Hospitalization** (possibly death)
- Vaccine failure - **Breakthrough** (full vacc. + hosp.)

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Support *complex tasks*:

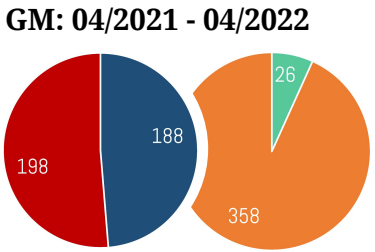
→ Locate problematic mutations (*prevention*)

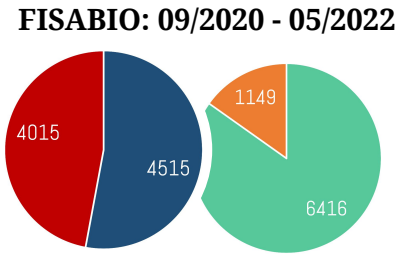
→ Extra information (*policy selection*)

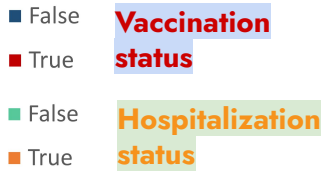
(among others)

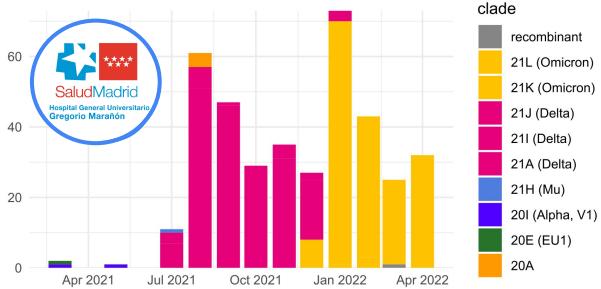
Data

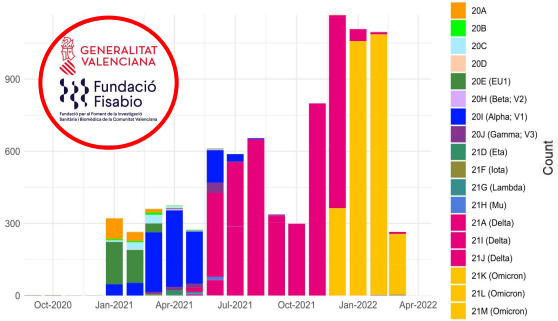
- Data sources: FISABIO (8.534) + GM hospital (386)
- Covariates: *sex*, *age*, *sample month* and *genomic sequences* (AA)
  - Hospitalization study: vaccination status as covariate

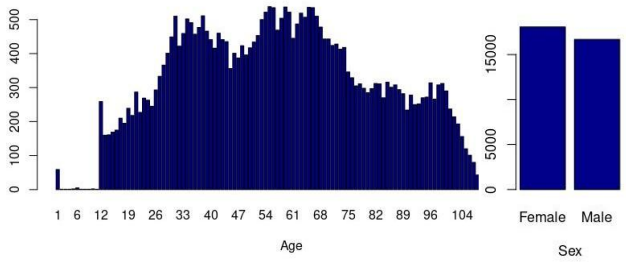












Preprocessing

- Clean the dataset:
  - Remove rows with >10% of missing values
  - Patients with partial information samples
  - Samples before 01/01/2021
  - Genome positions without mutations (at least >1 type of AA)

- Full preprocessing only for Spike protein

  → 331 Spike genome positions (out of 1.272)

  → 5.928 cases (out of 8.920)

Model

~ Laplace prior (*sparsity*)

- Logistic regression with Hierarchical Group Lasso regularization

$$\text{logit}[P(Y = 1|\mathbf{X})] = \beta_0 + \sum_{i=1}^{p} X_i\beta_i + \sum_{i<j} X_{i:j}\beta_{i:j}$$

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  - Negative log-likelihood loss function
  - *L1* reg. + *k*-fold CV regularization strength

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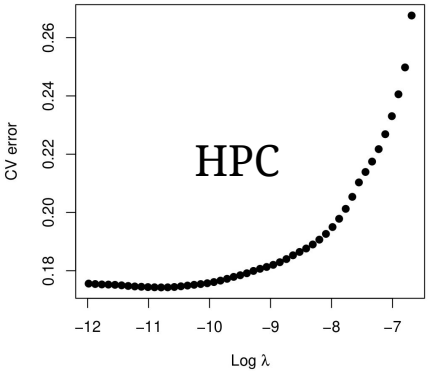

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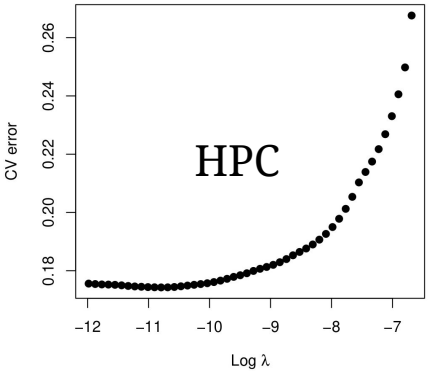

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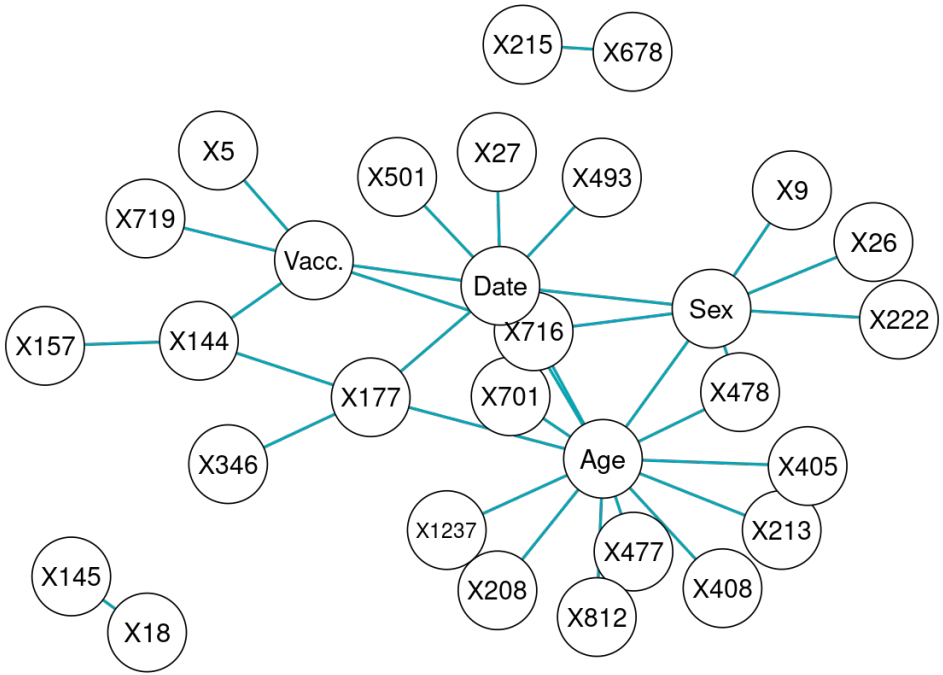
Strong hierarchy:

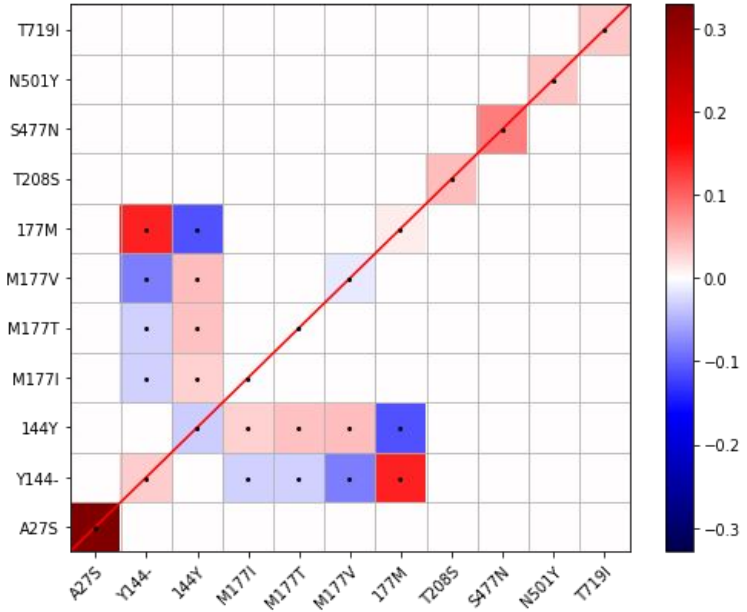
$$\beta_{i:j} \neq 0 \Rightarrow \beta_i \neq 0\,, \beta_j \neq 0$$

Overparametrization:

For each position, the sum of its main effects is 0, as well as for its interaction coefficients

Hospitalization results





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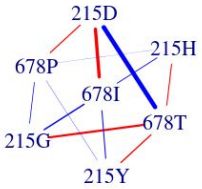

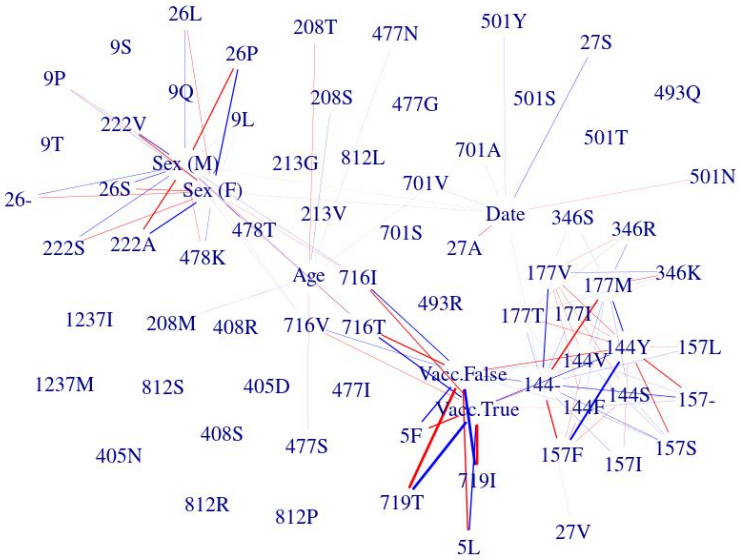

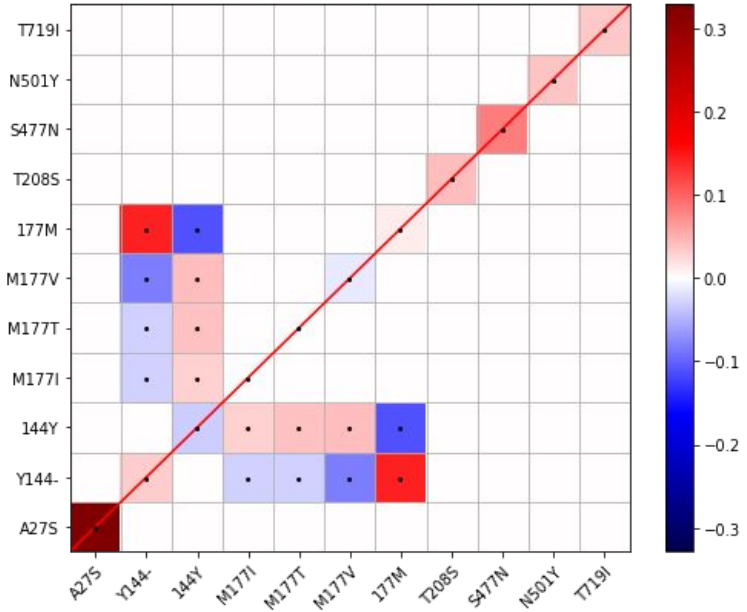

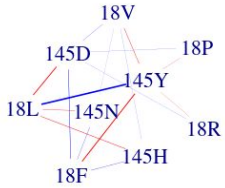

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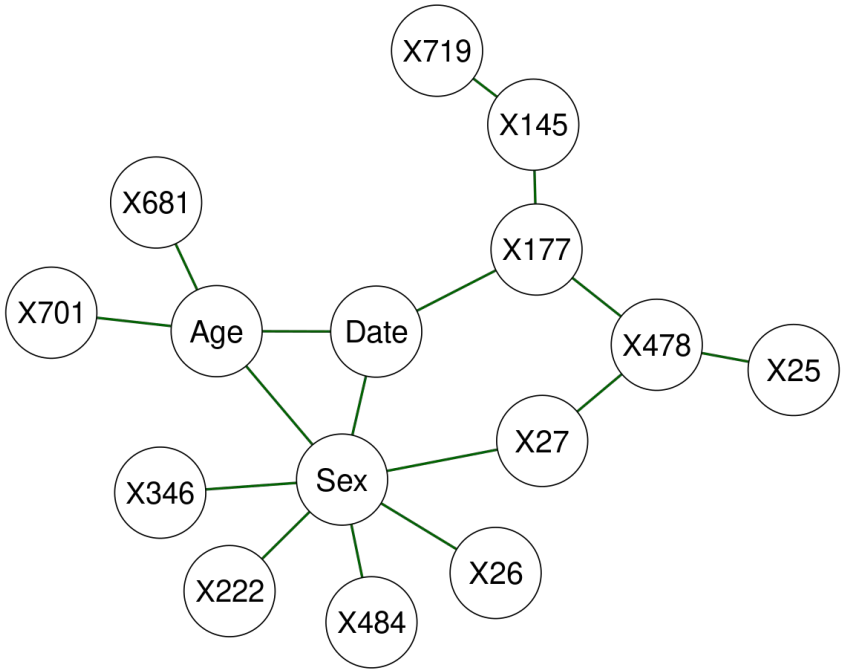

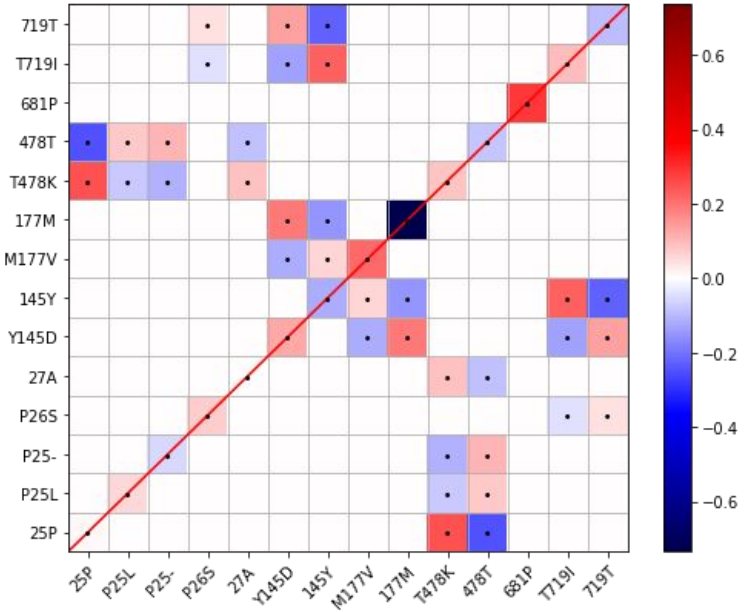

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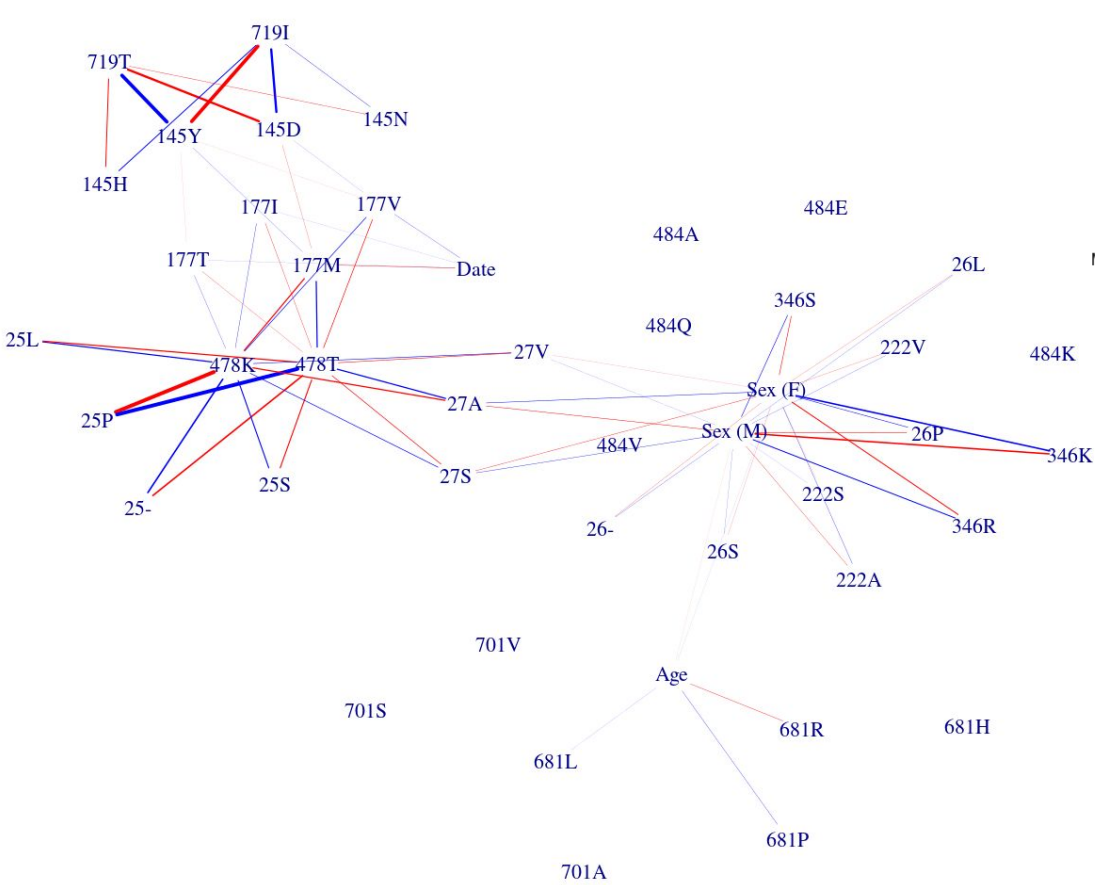

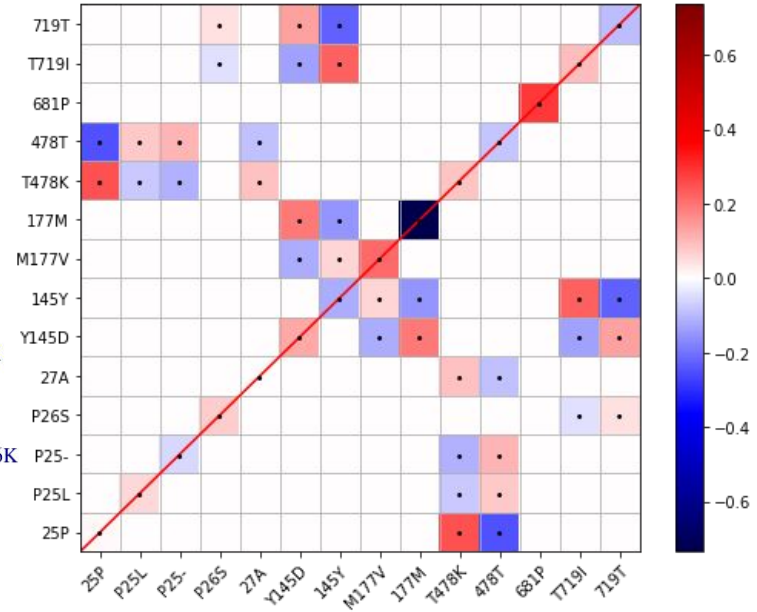

Conclusions

- Several novel interaction found, some of interest
- Effects of well-known mutations are enhanced or diminished by mutations in other positions
  - Example: **T478K** vs. **478T** in combination with **25P** (hosp.)
- Further analysis:
  - Remaining parts of the genome (ongoing)
  - Characterization of the effects of the preprocessing pipeline
  - Augment with other data sources (available)

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Thanks!

Reach out: simon.rodriguez@icmat.es