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

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Objective

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

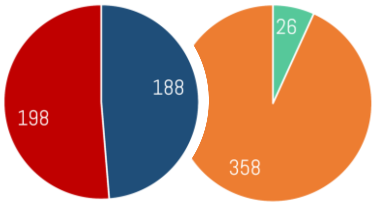
○ Severity - **Hospitalization** (possibly death)

○ Vaccine failure - **Breakthrough** (full vacc. + hosp.)

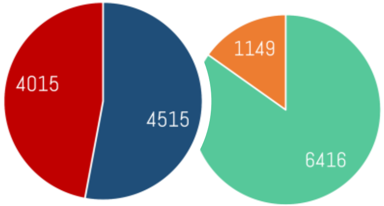
Data

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

GM: 04/2021 - 04/2022

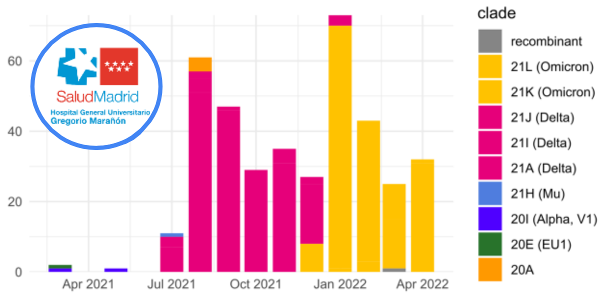


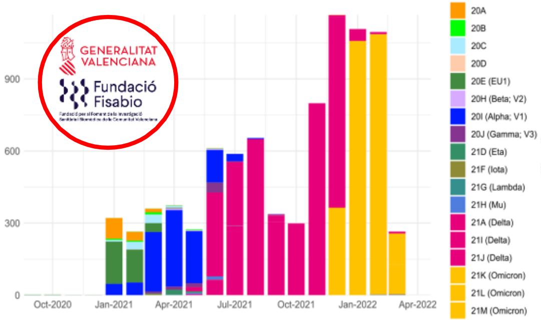
FISABIO: 09/2020 - 05/2022

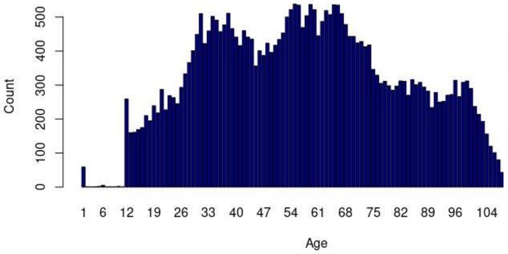


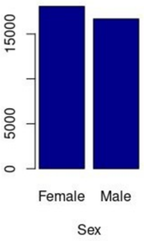
🟦 False
🟥 True
Vaccination status

🟩 False
🟧 True
Hospitalization status









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)

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- Preserve more data with imputation? Possible changes in the preprocessing?

Model

- 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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  - *L1* reg. + *k*-fold CV regularization strength

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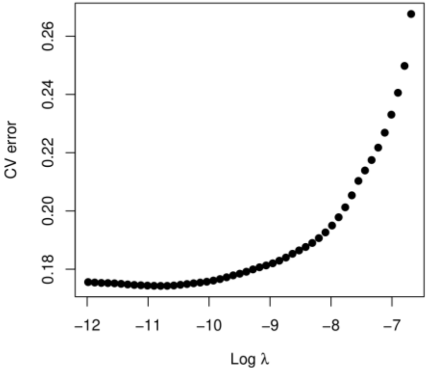

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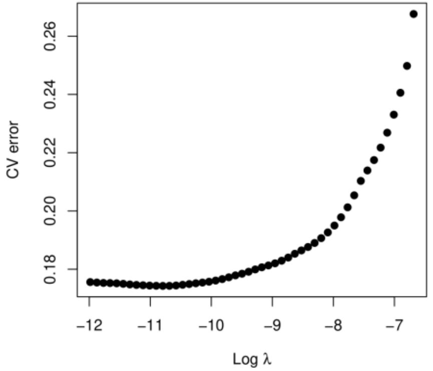

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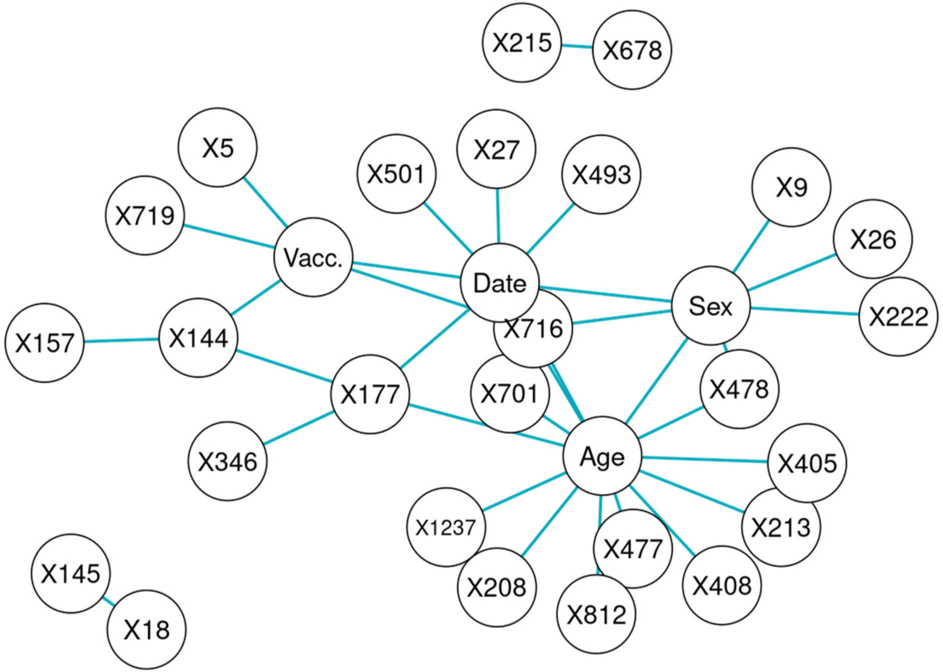
Strong hierarchy:

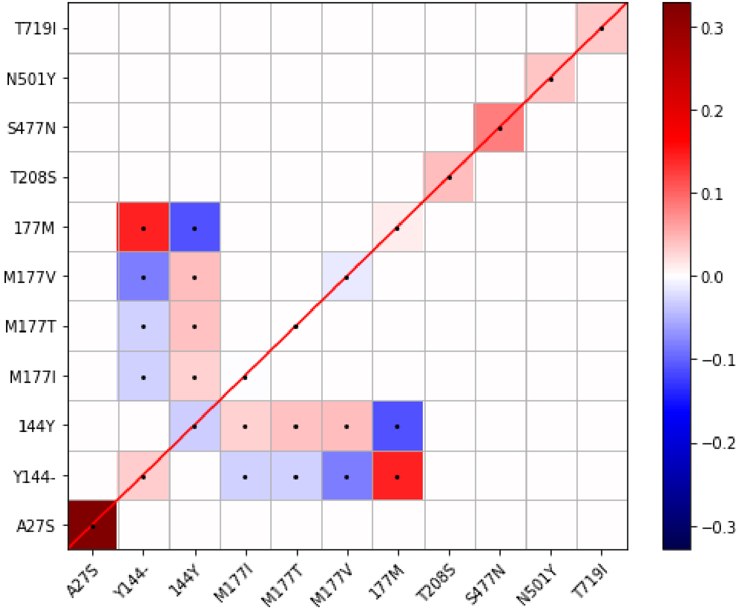
$$\beta_{i:j} \neq 0 \Rightarrow \beta_i \neq 0\,, \beta_j \neq 0$$

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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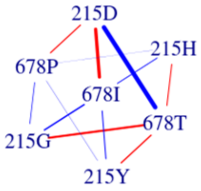
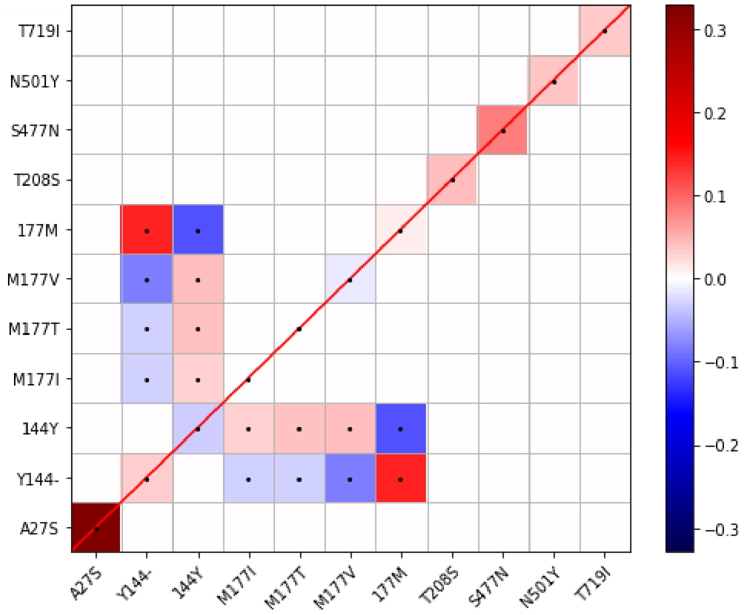
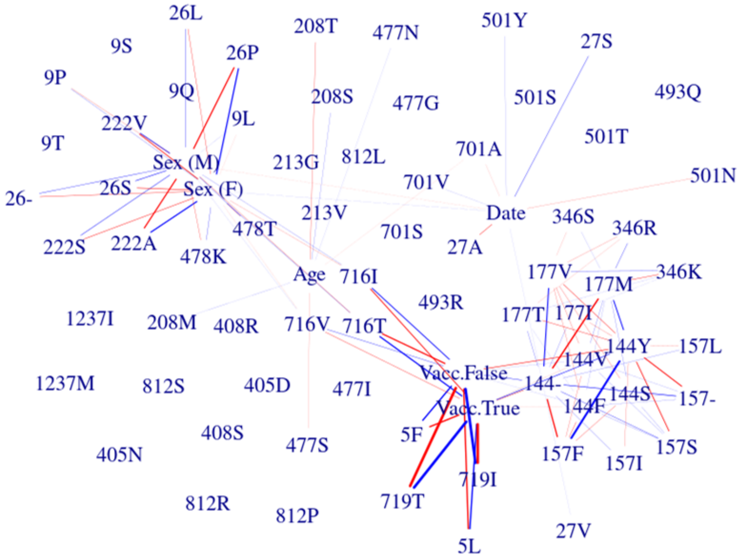
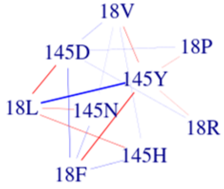
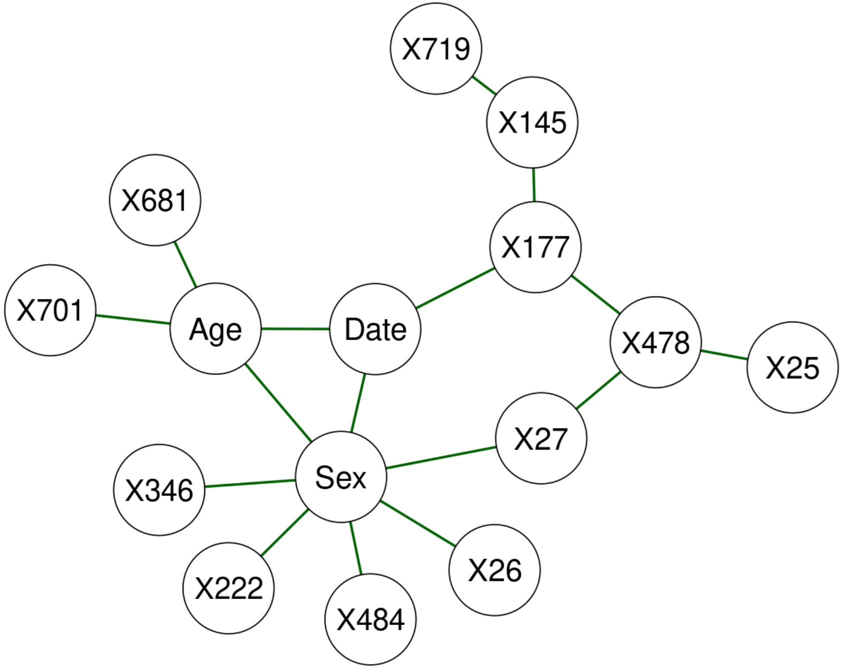


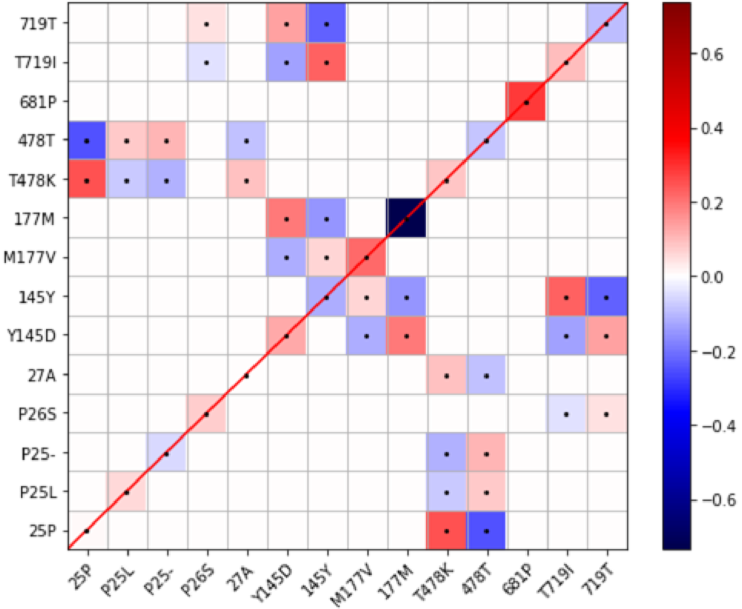






Breakthrough results





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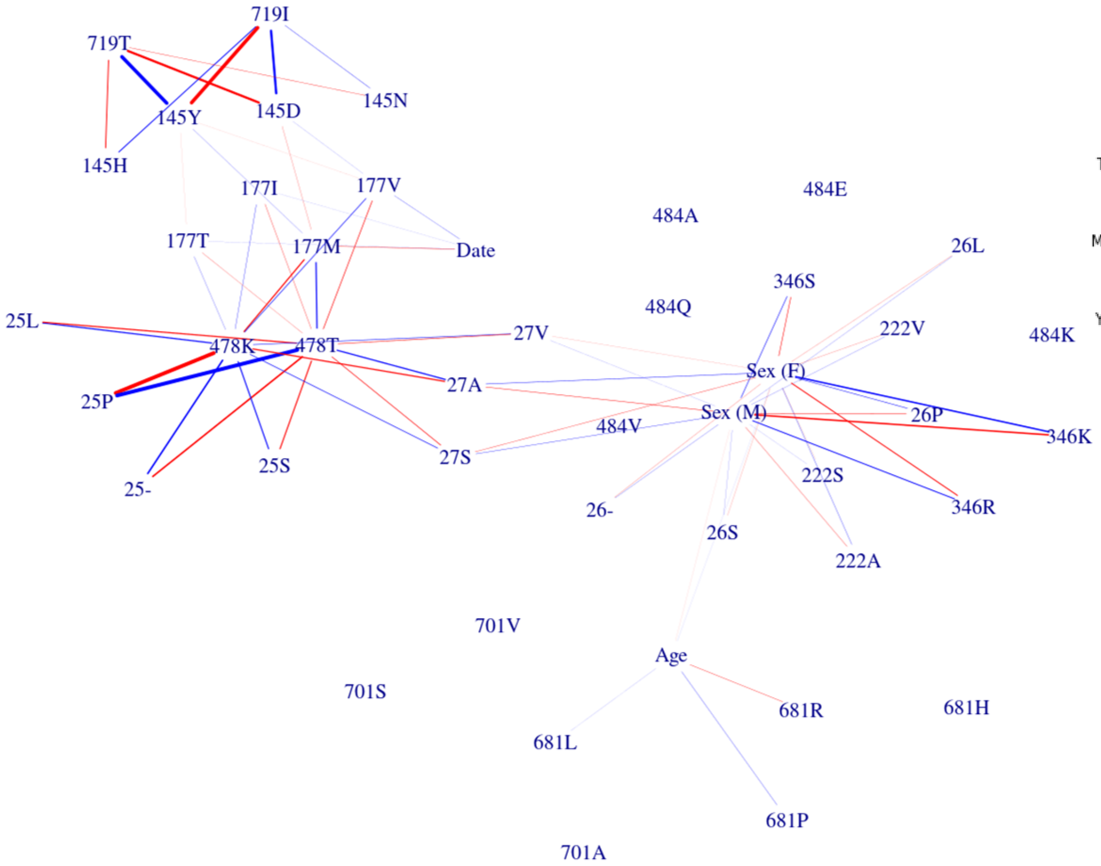

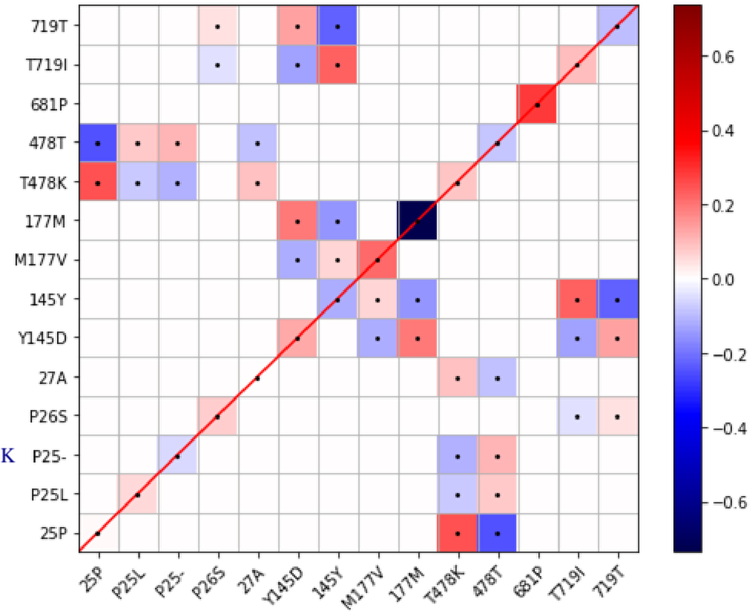

Conclusions

- 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
    - Characterization of the effects of the preprocessing pipeline
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Thanks!

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