



## Master project 2021-2022

### Personal Information

<b>Supervisor</b>	Bolognesi Benedetta
<b>Email</b>	bbolognesi@ibecbarcelona.eu
<b>Institution</b>	IBEC
<b>Website</b>	<a href="https://ibecbarcelona.eu/protein-phase-transitions-in-health-and-disease/">https://ibecbarcelona.eu/protein-phase-transitions-in-health-and-disease/</a>
<b>Group</b>	Phase Transitions in Health and Disease

### Project

## Computational genomics

#### Project Title:

Mapping Amyloid Nucleation by Deep Mutagenesis

#### Keywords:

Amyloid, Neurodegeneration, Combinatorial Libraries, Deep Mutational Scanning

#### Summary:

One common principle among all forms of dementia is the aggregation of specific proteins into insoluble amyloid aggregates that deposit in the brains of patients. These same proteins are also mutated in inherited forms of dementia. Our lab has developed an assay that allows to measure the ability of thousands of protein sequences in parallel to form new aggregates. In this project you will design, build, test and analyse massive mutational libraries (thousands of mutations) that encompass all possible mutations in the main proteins that aggregate in a number of neurodegenerative conditions (Alzheimer's, Parkinson's, ALS). The result of this approach will be mutational map(s) through which we are able to predict the impact of mutations in these proteins, i.e. to predict if people carrying those mutations are likely to develop dementia later in life or not. These maps will also be used to gather mechanistic insights on the process of amyloid nucleation, a fundamental biophysical process whose determinants are still unknown. The project combines experiments and computational analysis but it can be tweaked depending on your interest and ambition. Get in touch to discuss this!

#### References:

1. M Seuma, A Faure, M Badia, B Lehner, B Bolognesi\* The genetic landscape for amyloid beta fibril nucleation accurately discriminates familial Alzheimer's disease mutations. *Elife* 10, e63364 (2021) 2. Bolognesi B\*; Faure A; Seuma M; Schmiedel J; Tartaglia GG; Lehner B. The mutational Landscape of a Prion-like Domain. *Nature Communications* (2019) 10(1),4162.

#### Expected skills::

R, Python, Basic Molecular Biology (PCRs, gels)

#### Possibility of funding::

To be discussed

#### Possible continuity with PhD: :

To be discussed

**Comments:**

The project is flexible, meaning that the % of time dedicated to experimental or computational work can be tailored to the student's interest.

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