Deep mutational scanning of ubiquitin reveals evolutionary constraints

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First-year PhD students in the UCSF iPQB (Biophysics and Bioinformatics) program get a crash-course in being a scientist: they form teams to work on a real-life research project in the PUBS [1] class (Physical Underpinnings of Biological Systems). This class was originated by Dr. Jamie Fraser [2], building on Dr. Joe DeRisi [3]'s legendary ?team challenge? , and is currently directed by Dr. Martin Kampmann. One of the goals of PUBS is to publish the results from the class in a peer-reviewed journal. The second such publication, reflecting results from the 2015 and 2016 classes, just came out in Biology Open [4]. All students (including Kampmann lab Biophysics student Ruilin Tian [5]) are authors ? and the publication was led by first author David Mavor (now postdoc in the Bolon lab), who coordinated the PUBS research and analysis as a graduate student in the Fraser lab. The class used deep mutational scanning to investigate the protein ubiquitin. While ubiquitin is highly conserved in evolution, most residues can be mutated without decreasing fitness of yeast grown under standard conditions. When students screened a library of all point mutants of ubiquitin in yeast under different stress conditions, they revealed that almost every residue was essential under at least one stress conditioned. The students used various bioinformatics approaches to generate mechanistic hypotheses explaining the observed fitness landscape.


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