Engineering enzymes for biocatalysis and gene editing

Monica Neugebauer
University of California – Berkeley

Enzymes are Nature's catalysts with applications in energy, materials, drug manufacturing, and human health. Through protein evolution, we can reprogram enzymes to perform new and useful reactions, such as halogenation or gene editing. In my thesis work, I discovered a family of enzymes that halogenate unactivated C_{sp3}-H bonds, a challenging but important synthetic transformation. By performing biochemistry, X-ray crystallography, and high-throughput screening, we uncovered the mechanistic basis for regioselective halogenation within this enzyme family and used the resulting insights to engineer new halogenases with promising biocatalytic applications. In my post-doctoral work, I used continuous protein evolution to develop novel cytosine base editors that perform highly efficient editing of C•G base pairs to T•A base pairs within therapeutically relevant sites and cell types. These newly evolved base editors overcome some limitations of existing cytosine base editors and demonstrate the power of protein evolution for addressing challenges in biotechnology.