

Dr. Raluca Ostafe

“Ultra-high-throughput Screening Systems Based on Flow Cytometry and Microfluidic Devices for Directed Evolution of Different Enzyme Classes”

In the field of biotechnology, we are often employing enzymes to perform the tasks previously reserved for chemical catalysts. Enzymes have the advantages that they are environmentally friendly and are more specific compared to the chemical catalysts. However, it is not always possible to find in nature an enzyme that performs the exact reaction that is needed for the industrial process or that is active in the required conditions. Therefore, the natural properties of the enzymes often need to be tuned for specific process conditions by changing specificity, optimal reaction temperature, optimal pH or increasing activity. Enzymatic properties can be changed by means of directed protein evolution. Similar to the Darwinian evolution, directed evolution comprises of iterative cycles of mutations and selection and screening but at an accelerated speed. The main bottleneck in this type of experiments is the development of a screening method that can be used for the selection of an improved variant with the property of interest. The widespread used screening methods are based on micro-titer plates (MTPs) but they are expensive, laborious, time-consuming and only a small number of variants can be screened (103-106 in months). We have been focusing on establishing ultra-high-throughput screening (HTS) assays that can be used for screening mutant libraries using either fluorescence activated cell sorting or microfluidic devices. Using these improved methods more than 107 variants can be evaluated in much shorter timeframes (hours). The developed screening systems were successfully applied for the directed evolution of different enzymes like glucose oxidase, cellulases, xylanases, chitinases and peroxidases. All the chosen catalysts have numerous industrial applications ranging from biomedicine to biofuel industry.



I am a scientist with more than five years research experience and I feel that I have the expertise, training and motivation necessary to successfully fill out the proposed position. I have finished my PhD at the RWTH Aachen University (one of the six elite universities in Germany) and completed my PhD in May 2013 with high distinction with a thesis entitled “Development of High Throughput Screening Systems of Mutant Libraries for Sugar Degrading Enzymes (Glucose Oxidase and Cellulases)”. After the completion of my PhD research I have received a Postdoctoral fellowship in Prof. D. Weitz laboratory at the School of Engineering and Applied Sciences, Harvard University, Cambridge, Massachusetts, USA. Here I have used my molecular biology knowledge and applied it to developing screening systems for gene libraries based on microfluidic devices. I have moved back to Germany where I have received

a Group Manager position at Fraunhofer Institute for Molecular Biology and Applied Ecology (IME), Aachen. I was involved in writing, participating and managing various scientific projects that were collaborative between universities and industry and were focused on protein engineering for industrial biocatalysts. Throughout my career I have maintained close collaboration with West University of Timisoara (WUT), my alma mater. Here I was engaged in setting up a molecular biology laboratory by assisting in equipment procurement and training of personnel. Last year I have moved to Indiana Biosciences Research Institute, Indianapolis, USA where I am holding the position of Senior Staff Scientist. During this time I have set up new facilities for flow cytometry and production of microfluidic chips and was involved in developing of drug screening systems for cell assays for disease models. My research career was focused on molecular evolution of different enzymes, development of high-throughput screening systems based on flow cytometry and microfluidic devices, development of new enzymatic assays and production and purification of recombinant proteins from multiple host systems. I have extensive experience in molecular biology, creation of protein libraries, biochemical characterization of proteins, protein expression and purification, microbiology, cell biology, patient sample handling, blood cell types isolation, microfluidic chip development and production and cell compartmentalization methods. I have also worked in the fields of vaccine development, protein crystallization and metabolic engineering. During my career I was involved in the supervision of six intern students, one bachelor thesis, three master thesis and seven PhD thesis. In the past, students have been very active in all aspects of my research and I intend to continue this in the future. I published more than 15 peer-reviewed papers with another 7 submitted and a couple more in preparation. I also succeeded in getting three international patents issued. On the managerial level I secured significant funding for research and equipment, established new technologies and was involved in procurement with deadline and budget demands. My contributions for the molecular evolution research amounted to approximately three million USD coming either from projects supported by public funding or from industrial collaboration partners.

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