

JOINT EVENT

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Protein engineering applied to obtain biobetters of antitumor enzyme asparaginase**Gisele Monteiro, Costa I M, Costa-Silva T A, Effer B, Meira-Lima G, Biasoto H P, Silva C, Pessoa A and Rangel-Yagui C**
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Asparaginase (ASNase), an enzyme biotechnologically produced by bacteria, is one of the most important compounds in polychemotherapy to treat acute lymphoblastic leukemia (ALL) in children. There are only three options available as medicine: native enzyme from *Erwinia chrysanthemi* (ErA) or extracted from *Escherichia coli* (EcA) and formulated as native or PEGylated (PEG-EcA). However, these options yet present some problems in patients, such as to elicit hypersensitivity and allergic reactions, neurotoxicity, and hyperammonemia. Aiming to avoid some of these problems, our research group has developed several different mutant proteoforms, expressed in bacteria and yeast, in periplasmic or secreted to extracellular space; with improvement in specific activity, kinetic parameters and stability; different oligomerization states, glycosylated or not, through engineering of genes from *E. coli*, *E. chrysanthemi* and *S. cerevisiae*. We obtained mutants from *E. coli* ASNase more resistant to human proteases and less immunogenic. In relation to *E. chrysanthemi* enzyme, our mutants present higher asparaginase activity than the native form, with improved kcat. In addition, we obtained strains of *Pichia pastoris* that express glycosylated ASNases from bacteria. Last but noteworthy, we obtained *P. pastoris* and *E. coli* strains that express active ASNases from *S. cerevisiae*, an eukaryotic promising options to replace bacterial formulations.

Biography

Gisele Monteiro has completed her PhD at the University of São Paulo in Molecular Biology. Currently, she is an Associate Professor of Pharmaceutical Biotechnology in the Faculty of Pharmaceutical Sciences (FCF/USP) and the Vice-Coordinator of the Graduate Course in Biochemical-Pharmaceutical Technology. She has published more than 20 papers in reputed journals and has been serving as an Associate Editor of Brazilian Journal of Microbiology. She received 10 scientific awards, national and international. Her main scientific interest is the study of antitumor drugs and the engineering of proteins used as biopharmaceuticals, such as asparaginase.

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