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ProxiMAX randomization: Precision protein engineering

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ProxiMAX randomization is the technology that lies behind Isogenica's Colibra™ offering. It is a defined saturation mutagenesis process that delivers precision control of both identity and relative ratio of amino acids at specified locations within a protein/antibody library. Thus unwanted amino acids such as cysteine and methionine can be eliminated from libraries because no constraints are imposed by the genetic code. Moreover, the process is non-degenerate, which means that encoding DNA libraries are as small as is physically possible. ProxiMAX relies on a process of saturation cycling comprising ligation, amplification and digestion for each cycle and is the science behind the commercial Colibra™ technology. Currently focused on antibody libraries but with achieved diversities of >99% (6 & 11 saturated codons) and the potential to generate libraries of up to 10^{14} components, we contest that ProxiMAX randomization is a vital tool in engineering any protein library of the highest quality. This presentation will examine the development of the ProxiMAX process and give examples of libraries created to date.

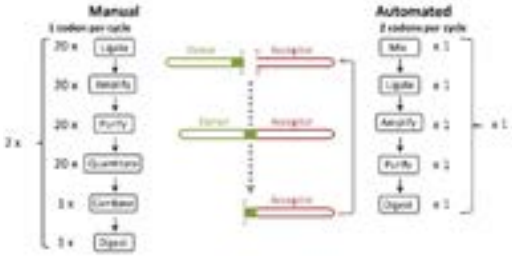

Figure 1: Overview of the ProxiMAX

Recent Publications

1. Ferreira Amaral M M, Frigotto L and Hine A V (2017) Beyond the natural proteome: nondegenerate saturation mutagenesis - methodologies and advantages. Meth. Enyzmol. 585:111-133.
2. Frigotto L, Smith M E, Brankin C, Sedani A, Cooper S E, Kanwar N, Evans D, Svobodova S, Baar C, Glanville J, Ullman C G and Hine A V (2015) Codon-precise, synthetic, antibody fragment libraries built using automated hexamer codon additions and validated through next generation sequencing. Antibodies 4:88-102.
3. Chimonides G F, Behrendt J M, Chundoo E, Bland C, Hine A V, Devitt A, Nagel D A and Sutherland A J (2014) Cellular uptake of ribonuclease A functionalised core–shell silica microspheres. J Mater Chem B, 2:7307-7315.
4. Nagel D, Behrendt J M, Chimonides G F, Torr E E, Devitt A, Sutherland A J and Hine A V (2014) Polymeric microspheres as protein transduction reagents. Mol. Cell Proteomics, 13:1543-1551.
5. Ashraf M, Frigotto L, Smith M E, Patel S, Hughes M D, Poole A J, Hebaishi H R M, Ullman C G and Hine A V (2013) ProxiMAX randomisation: a new technology for non-degenerate saturation mutagenesis of contiguous codons. Biochem. Soc. Trans. 41:1189-1194.

Biography

Anna V Hine studied at the University of Manchester (UK) and Harvard Medical School. She is a Reader and Associate Dean Enterprise at Aston University (UK). In March 2013, she was named BBSRC Commercial Innovator of the Year 2013, for her work in transferring ProxiMAX randomization into SME Isogenica Ltd. She is a Molecular Biologist by training, she relishes interdisciplinary work.

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