

Astex announces structure-based drug development program on cytochrome P450

Cambridge, UK, 3 May, 2001 - Astex Technology, the structure-based drug discovery company, today announced a major research program aimed at elucidating the crystal structures of key human cytochrome P450 proteins. These structures will assist pharmaceutical partners to rationally optimize their lead compounds and reduce attrition rates in drug development programs. Astex has recruited José Cosme, PhD, and Pamela Williams, PhD, who were both involved in solving the first crystal structure of a mammalian cytochrome P450, to lead the research program.

Cytochrome P450 enzymes are the most prominent group of drug-metabolising enzymes in humans, and consequently are of great importance to the pharmaceutical industry. Since cytochrome P450s were first linked to drug metabolism in the 1970s, many drugs have had to be withdrawn from the market or stopped in clinical trials due to adverse side effects from their interactions with these enzymes. In addition, it is known that certain individuals and populations in the world have different forms of these enzymes and hence react differently to the same drugs. Astex will use its proprietary High Throughput X-ray crystallography (HTX?) technology to rapidly determine the three dimensional structures of cytochrome P450s. This will allow rational and effective optimisation of lead compounds and improve their pharmacokinetic properties.

Dr Cosme joins Astex from The Scripps Research Institute, California, USA. Prior to this, Dr Cosme obtained his PhD in Molecular Toxicology, in 1995, from the University of Paris XII, France, with high honours 'Summa cum Laude'.

Dr Williams joins Astex from the University of Oxford, UK, where she worked on enzyme structure determination. Prior to this, Dr Williams was a postdoctoral research assistant at The Scripps Research Institute and obtained her DPhil in Molecular Biophysics in X-ray protein crystallography from the University of Oxford in 1996.

"Cytochrome P450s are an extremely important class of enzymes that can metabolise potential drug candidates," commented Harren Jhoti, PhD, Co-founder & CSO of Astex. "By defining their three dimensional structures we will help our corporate partners to accelerate the drug discovery process and reduce attrition rates during development."

Astex Technology is a structure-based drug discovery company pioneering the use of High Throughput X-ray crystallography (HTX?) for the rapid identification of novel drug candidates. HTX? is part of an integrated drug discovery platform that includes



cutting-edge technologies covering all aspects of structure-based research, including protein production, crystallization, structure determination, bioinformatics and computational and medicinal chemistry. Astex is using this drug discovery platform to identify novel lead compounds for proprietary and public domain targets and has established strategic collaborations with major pharma. Astex was formed by leading industrial and academic scientists and is based at the Cambridge Science Park, UK.

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