The FDA requires that the absolute stereochemistry of any chiral drugs be determined for regulatory submission. However, chiral compounds may often prove to be the most desirable drug candidate. Thus reliable methods for establishing the absolute stereochemistry of these candidates are essential within the pharmaceutical industry. It has been known for many years that the absolute stereochemistry of structures can be determined by a single crystal X-ray diffraction anomalous dispersion experiment [1]. For structures containing atoms heavier than sulphur this process is fairly straightforward and can be carried out on a standard laboratory Mo Kα diffractometer. However, for structures consisting only of light atoms the process can prove more complex. In the work presented the use of single crystal x-ray diffraction for establishing the absolute structure of both light and heavy atoms will be discussed. This will include the use of the well-known Flack parameter [2] and a new method created by Hooft, Straver and Spek for determining the absolute structure of chiral compounds based on the Bijovet pair intensity differences and accessible via the program Platon [3].

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MS21 O4

Crystallochemical, vibrational and optic Studies of the silver doped $NaY(PO_3)_4$ structure. M. El Masloumi[a], (b), V. Jubéra[a], S. Pechev[a], J. P. Chaminade[a], J. J. Videau[a], M. Mesnaoui[b], M. Maazaz[b], B. Moine[c].
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Keywords : Crystal structure ; Phosphate ; Silver luminescence ; decay time

Since ten years, the study of the optical properties of monovalent silver phosphates was undertaken by the LCSM of Marrakech (Morocco) in collaboration with the ICMCB (France), these investigations related to the well crystallize materials as vitreous [2]. It made it possible to identify three centers of luminescence covering the whole of the visible one.
The aim of this work is, on the one hand, to widen the range of the compositions crystallized in order to facilitate a deepening of the comprehension of the mechanisms of luminescence of the various types of association of the ions Ag^+ while optimizing the output of photoluminescence and on the other hand, to associate the silver ions rare earth in new phosphates (crystals and glasses), in seen to examine their mutual influences (creation of new centers, transfer of energy between centers, interaction between silver clusters and ions rare earth, etc.) and to understand the mechanisms of them.
It is in this context that the structure $NaY(PO_3)_4$ in single-crystal form, could be established by diffraction of X-rays (**$P2_1/n$**).This phase will enrich the family by the metaphosphate of general formula $NaLn(PO_3)_4$ (**Ln = La**[3]**, Nd, Gd, Er**).A comparative study of the influence of rare earths on the structure could be carried out and interpreted.
In parallel, the study of luminescence carried out on crystals of composition $Na_{0.9}Ag_{0.1}Y(PO_3)_4$ showed two types of emission. Measurements of declines of luminescence make it possible to advance mechanisms of fluorescence of the silver

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MS01 P06

A boron based antifungal agent in complex with its target protein domain

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Keywords: leucyl-tRNA synthetase, drug design, onychomycosis

Aminoacyl-transfer RNA (tRNA) synthetases, which catalyze the attachment of the correct amino acid to its corresponding tRNA during translation of the genetic code, are proven antimicrobial drug targets.
Recently, we showed that the broad-spectrum antifungal 5-fluoro-1,3-dihydro-1-hydroxy-2,1-benzoxaborole (AN2690), which is in development for the treatment of onychomycosis and inhibits the fungal leucyl-tRNA synthetase (LeuRS), also binds to bacterial LeuRS by formation of a stable LeuRS-AN2690 adduct in the editing site of the enzyme. Adduct formation is mediated through the boron atom of AN2690 and the 2'- and 3'-oxygen atoms of tRNA's3'-terminal adenosine. The trapping of enzyme-bound tRNA in the LeuRS editing site prevents catalytic turnover, thus inhibiting synthesis of leucyl-tRNA and consequentially blocking protein synthesis [1].
We now present x-ray structures of a fungal LeuRS editing domain, the real drug target, alone and in complex with a similar adduct. Together with our low resolution x-ray structure of the human LeuRS editing domain (3.1 Å) and homology modeling results, these data open the way for rational drug improvement.

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MS04 P17

The Center for Structural Molecular Biology (CSMB) at Oak Ridge National Laboratory (ORNL) G.W. Lynn W.T. Heller, A. N. Raghavan, V. S. Urban, K.L. Weiss, Y. Mo and D.A.A. Myles, *Chemical Sciences Div. ORNL, Oak Ridge, TN 37831*. E-mail: lynngw@ornl.gov

Keywords: small-angle neutron scattering, biology, biomembranes,

The CSMB at ORNL is developing facilities and techniques for the characterization and analysis of biological systems at the High Flux Isotope Reactor (HFIR) and the Spallation Neutron Source (SNS). The cornerstone of the effort is a small-angle neutron scattering instrument (Bio-SANS) at HFIR that will be dedicated to the analysis of the structure, function and dynamics of complex biological systems. In support of this program, we are developing advanced computational tools for neutron analysis and modeling, alongside a supporting biophysical characterization and X-ray scattering infrastructure. Specifically, we established a Bio-Deuteration Laboratory for *in vivo* production of H/D labeled macromolecules that will permit selected parts of macromolecular structures to be highlighted and analyzed *in situ* using neutron scattering. The CSMB is also expanding our efforts to include the study of biomembranes by neutron reflectometry. These new facilities will make ORNL a world-leading scientific center and user facility for neutron-based studies of bio-molecular structure and function.

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MS04 P18

Structure of IgNAR single domain antibody and *Plasmodium falciparum* AMA1 complex Victor Streltsov[a], Kylie Henderson[a,b,c], Andrew Coley[b,c], Olan Dolezal[a], Adrian Batchelor[d], Vincent Murphy[c], Robin Anders[3], Michael Foley[b,c], Stewart Nuttall[a]. [a]*CSIRO Molecular and Health Technologies, Melbourne, Australia.* [b]*Cooperative Research Centre for Diagnostics, Brisbane, Australia.* [c]*School of Biochemistry, La Trobe University, Melbourne, Australia.* [d]*University of Maryland School of Pharmacy, Baltimore, Maryland, USA.* E-mail: victor.streltsov@csiro.au

Keywords: three-dimensional protein structure; antibody antigen complexes, biological macromolecular crystallography

Apical Membrane Antigen-1 (AMA1) is essential for red blood cell invasion by *Plasmodium* parasites and is a leading malarial vaccine candidate. However in humans several infection cycles are required to establish AMA1-specific protective immunity due to extensive polymorphisms within the protein's surface-exposed loops. Using an AMA1-specific IgNAR (Immunoglobulin New Antigen Receptors) single variable domain antibody as starting material, we performed targeted mutagenesis and iterative selection against AMA1 proteins from *Plasmodium falciparum* strains 3D7, W2mef, and HB3. We present the co-crystal structures of two resulting antibody-AMA1 complexes, which reveal the extended IgNAR CDR3 (Complimetarity Determining Region) loops penetrating deep into a hydrophobic cleft on the antigen surface, and contacting residues conserved across parasite species. Comparison of a series of CDR3-based affinity-enhancing mutations allowed dissection of the relative contributions to binding kinetics of various CDR3 – AMA1 contacts, and correlation of these affinities to inhibition of parasite red blood cell invasion. Taken together, these findings and structures provide insights into the mechanisms of single-domain antibody binding, and will enable future design of reagents which target otherwise cryptic epitopes in apicomplexan parasites.

MS04 P19

X-ray Absorption Spectroscopy Study of Copper Binding to β–Amyloid Peptide Victor Streltsov[a], Kevin Barnham[b], Jose Varghese[a], [a]*CSIRO Molecular and Health Technologies, Melbourne, Australia.* [b]*University of Melbourne, Melbourne, Australia.*
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Keywords: beta-amyloids, copper proteins, EXAFS

While the causes of Alzheimer's disease (AD) are still uncertain, the deposition of misfolded protein, described as amyloid plaque, is considered as defining pathological feature of AD. The major constituent of AD plaques is the β-amyloid peptide (Aβ) that is cleaved from the membrane-bound amyloid precursor protein. *In vitro*, Aβ binds metal ions including Cu^{2+} giving rise to extensive redox chemical reactions. Since elevated levels of Cu are found in amyloid deposits in AD affected brains, the oxidative stress causing cellular damage may be related to the production of reactive oxygen species by metallated forms of Aβ [1,2]. A number of studies indicated that the coordination sphere around the Cu ions is nitrogen rich and different types of coordination has been proposed for ligands to Cu ions in Aβ Cu complexes. The intrinsic propensity of Aβ to self-association creates experimental obstacles and may lead to different Cu binding geometries observed. Preparation of protein samples with structural homogeneity is critical [3]. A series of X-ray Absorption Spectroscopy (XAFS) studies on β–Amyloid peptide Cu complexes under a range of conditions are presented.

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MS06 P12

Facilitating Low Volume Protein Crystallography Set-ups Using the mosquito® Liquid Handler. Joby Jenkins, Rob Lewis, Jas Sanghera, Chloe Milburn
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