Nota Técnica / Technical Note

The ALBA Synchrotron:

techniques useful for the study of biological samples and medicines

ABSTRACT:

This OPA technical note presents the techniques of the ALBA Synchrotron focused on the study of biology and biomedicine at the beamlines MISTRAL, XALOC and MIRAS. ALBA is the only synchrotron light source existing in Spain and use the high quality synchrotron light to understand the structure of materials in different scientific and industrial challenges such as the SARS-CoV-2 virus amongst many others. Its cutting-edge techniques offer clear advantages over conventional techniques.

RESUMEN:

Esta nota técnica de OPA presenta las técnicas del Sincrotrón ALBA centradas en el estudio de la biología y la biomedicina en los laboratorios de luz sincrotrón MISTRAL, XALOC y MIRAS. ALBA es la única fuente de luz sincrotrón que existe en España y utiliza la luz sincrotrón de alta calidad para proporcionar información acerca de la estructura de los materiales en diferentes desafíos científicos e industriales, como el virus SARS-CoV-2, entre muchos otros. Sus técnicas de vanguardia ofrecen claras ventajas sobre las técnicas convencionales.

PRESENTATION

The ALBA Synchrotron (www.albasynchrotron.es) is the only synchrotron light source that exists in Spain. It is managed by CELLS, a public consortium funded in equal parts by the Spanish and Catalan governments and started its operation in May 2012 (Figure 1).

ALBA Synchrotron is a facility that currently serves more than 2,100 academic and industrial researchers per year that use their cutting-edge techniques to perform top notch academic and industrial research. Around 5,000 hours of synchrotron light are produced per year used by its 8 beamlines or laboratories . Two additional beamlines are expected to start operation by the end of 2020.

Synchrotron light is ideal to visualize and analyze the structure and properties of all types of materials ranging from pharmaceuticals, advanced materials, nanotechnology, energy or batteries achieving enhanced results compared with the conventional techniques.

This technical note will briefly overview three of the beamlines dedicated specifically to the study of biological and biomedical materials named MISTRAL, XALOC and MIRAS.

Figure 1. Aerial view of the ALBA Synchrotron Light Source located in Cerdanyola del Vallés (Barcelona, Spain).

MISTRAL: THE SOFT X-RAY MICROSCOPE BEAMLINE

MISTRAL is a full-field Transmission X-ray Microscope that works from 270eV to 1200eV dedicated to perform cryo nano-tomography in the water window. The optical layout includes single-reflection elliptical glass capillary condenser, an objective Fresnel Zone plate (of 25 or 40 nm outermost zone widths) and a CCD camera. The spatial resolution in 2D is 30 nm and ~50 nm for tomography.

All these technical capabilities allow the visualization of cells in 3D without the need of slicing or dyeing the cells. Several interesting experiments have been performed at MISTRAL such visualizating how anticancer compounds migrate inside the cells which would otherwise be difficult if the cells had to be sliced as required by conventional microscopy; the observation of the exact location of nanoparticles used in drug delivery inside the cells; the determination of the effect of hepatitis C virus in the structure of the cell and also their subsequent structural recovery when the appropriate drug is delivered in the cell (Figure 2). This technique could be very valuable to decide whether a certain drug must or must not be tested in-vivo, which could save costs and time.

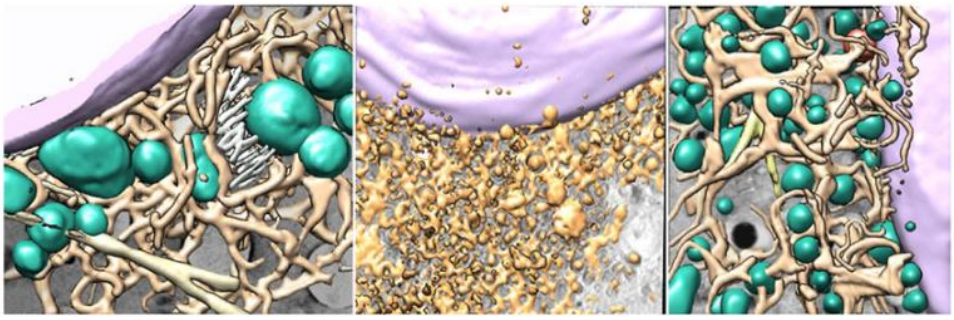

Figure 2. Interior of the healthy cell (left), interior of the cell affected by the hepatitis C virus (centre) and interior of the cell after treatment with antiviral drugs. Cell nucleus (violet), healthy mithocondria (green), healthy endoplasmic reticulum (beige) and altered endoplasmic reticulum (yellow). DOI: 10.1021/acsnano.6b01374

XALOC: THE MACROMOLECULAR CRYSTALLOGRAPHY BEAMLINE

The main XALOC optical elements are: a diamond window, a removable diamond filter (which could also be used as a Laue monochromator), a channel-cut monochromator and a Kirkpatrick-Baez (KB) focusing system. Other optical elements include white beam attenuators, slits, photon shutter, fluorescent screens and x-ray beam positioning monitors. The energy at XALOC ranges from 4.6 to 23 keV, the beam size at sample position is adjustable between the values 50-300 (H) x 6-100 (V) μm^2.

Macromolecular crystallography is an important and powerful technique used by pharmaceutical companies in the discovery process of new medicines as it allows the determination of the crystal structure of large macromolecules such as proteins, DNA or complexes attached to drugs. XALOC allows

the characterization of the specific interactions of a particular drug with its protein target at the atomic level through the detailed analysis of crystal structures of protein-ligand complexes in a fast and reliable way. XALOC has been used to design and improve drugs for the treatment of several diseases such as malaria, sleeping sickness (Figure 3) or HIV, amongst many more, and will help to test the efficiency of different drugs against virus such as SARS-CoV-2.

XALOC can be operated by remote control where samples are sent to ALBA facility and the data are collected without the need to be present at ALBA.

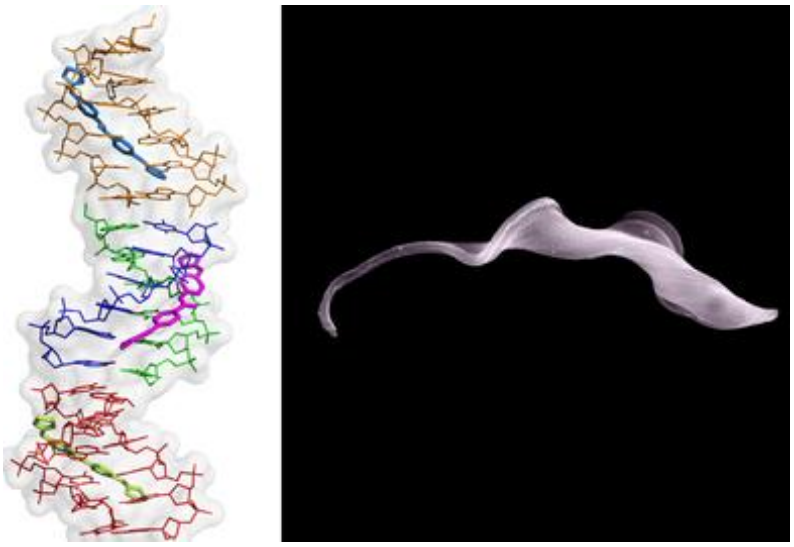

Figure 3. Left: 3D structure obtained at XALOC beamline of three drug molecules (blue, pink and phosphorescent green) perfectly linked to kinetoplast DNA of the parasite altering parasite normal function. Right: Trypanosoma brucei parasite responsible of African trypanosomiasis or sleeping sickness (photo: Dr. Leandro Lemgruber). DOI: 10.1093/nar/gkx521

MIRAS: THE INFRARED MICROSPECTROSCOPY BEAMLINE

MIRAS provides to their users a modern synchrotron-based infrared spectrometer and microscope capability covering a wavelength range from about 1 μm to ~100 μm with a spectral region optimized initially for investigation between 2.5-14 μm.

MIRAS is devoted to Fourier Transform Infrared (FTIR) spectroscopy and microscopy which is a very potential tool to identify the vibrational signatures and therefore the chemical composition of materials. It has been used to study the biochemical structure of human and animal tissues such as hair, skin, bone, brain, etc. and the effect of different drugs and cosmetics on the lipids, protein and DNA biochemical composition of the tissues.

CONCLUSIONS

ALBA is a synchrotron light facility which incorporates the latest technologies available, in operation since 2012. It provides the Spanish scientific and industrial community an invaluable tool for science and innovation becoming one of the flagships elements of Spanish science and technology landscape. Several of ALBA beamlines have applications in biomedicine such as in drug discovery (XALOC), determining the effects of a virus, bacteria and drugs on the cell structure (MISTRAL) and characterizing the structure of human and animal tissues and the effects of drugs and cosmetics on them (MIRAS). The different techniques, laboratories and the in-house expertise of ALBA are available for the industrial and scientific community to enhance their research and development activities. The industrial services may include mail-in, pre and post experiment support, data treatment, experimental reports, advice on synchrotron techniques, etc.

For more information about the different possibilities under those services, please visit our website (https://www.cells.es/en/industry/services) or contact our Industrial Liaison Office: industrialoffice@cells.es

