Industrial applications at the national synchrotron light source

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Synchrotron light provides an unique source of non-destructive methods for material characterization. At the National Synchrotron Light Source the industrial program benefits from a large collection of tools to analyze a wide range of materials. Embracing spectroscopic and diffraction methods it is possible to characterize a sample from molecular to atomic levels. Diffraction powder and macromolecular crystallography are typical examples providing useful tools for drug design. X-ray absorption spectroscopy are widely used by our industrial users in their quest to develop better batteries and catalysis studies. Specific examples will be presented and discussed in light of the needs of the industrial researcher.

Keywords: synchrotron, industrial applications, spectroscopy, diffraction

The particular mechanisms of DNA recognition and dimerization of MITF

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The Microphthalmia-associated Transcription Factor (MITF) is a key regulator of the expression of pigment-cell specific genes in melanocytes, the mature pigment producing cells of the skin and hair follicles. Moreover, in the past few years, MITF became one of the most studied macromolecule in the investigation of the mechanisms leading to melanoma, a particular skin cancer.

MITF is a member of the superfamily of basic Helix-Loop-Helix leucine zipper transcription factors (b-HLH-Zip). Like other b-HLH-Zip factors, MITF can bind a subset of the canonical palindromic E-box sequence (CANNTG) as well as related asymmetric motifs like the M-box (TCATNTG); nevertheless the exact mechanism in which MITF recognizes the correct promoters of target genes is not yet fully elucidated. Within the b-HLH-Zip family, MITF can associate with the Tfe factors, but no heterodimeric complexes containing MITF and the related Myc, MAX or USF-1 have been observed, raising the question how this discrimination is achieved.

We solved three crystal structures: the one of MITF in absence of DNA and two structures of MITF in complex with DNA duplexes encompassing two different target motives (E-box and M-box). In addition, we analyzed interactions between these DNA motives and several MITF mutants with documented phenotypes in mice, using different techniques such as Isothermal Titration Calorimetry, Transactivation assays and EMSA. The comparison of our structural, biophysical and functional data together with available biological data reveals the particular mechanism of DNA recognition by MITF and how MITF discriminates between the E and M boxes. In addition, our data demonstrate an unusual mode of dimerization that might explain how MITF selects its heterodimerization partners.

Keywords: transcription, DNA, interactions.