OXIDOREDUCTASES IN CELLULAR DEFENSE AND SIGNALING. SEARCH OF INHIBITORS FOR THERAPEUTIC PURPOSES

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PROFILE

Our current research is focused on the enzymology and molecular biology of oxidoreductases involved in mechanisms of cellular defense and signaling. We are investigating members of three oxidoreductase superfamilies participating in the metabolism of carbonyl compounds, along with other biological functions: aldo-keto reductases (AKR), medium-chain dehydrogenases/reductases (MDR) and aldehyde dehydrogenases (ALDH). We are especially interested in enzymes acting on the metabolism of signaling molecules (retinoids and prostaglandins) and associated with different human disease states, such as cancer and diabetes. Some of these enzymes are also phase I-drug metabolizing enzymes and are induced under oxidative stress, being responsible for developing tumor resistance to chemotherapy. Thus, they are relevant drug targets and are well suited for the design of selective enzyme inhibitors with potential use as pharmacological agents. Some illustrative examples of the enzymes being studied are zeta-crystallin, an RNA-binding protein involved in the cellular stress response; pro-apoptotic p53-induced gene protein 3 (PIG3); and aldo-keto reductase 1B10 (AKR1B10), a highly efficient retinaldehyde dehydrogenase which is induced in several types of cancer.

RESEARCH

RESEARCH INTERESTS

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MAIN RESEARCH LINES

Role of aldehyde dehydrogenases and aldo-keto reductases in retinoic acid metabolism. Development of enzyme inhibitors and drug discovery in cancer and diabetes research.

Techniques: enzyme kinetics, HPLC, mammalian cell culture, molecular modeling, protein purification, recombinant DNA, fluorimetry and UV-visible spectrophotometry, X-ray crystallography.

LAB FEATURED PUBLICATIONS

Pequerul R, Vera J, Giménez-Dejoz J, Crespo I, Coines J, Porté S, Rovira C, Parés X, Farrés J (2020) Structural and kinetic features of aldehyde dehydrogenase 1A (ALDH1A) subfamily members, cancer stem cell markers active in retinoic acid biosynthesis. Arch Biochem Biophys 681:108256.

Rivas A, Pequerul R, Barracco V, Domínguez M, López S, Jiménez R, Parés X, Alvarez R, Farrés J, de Lera AR. (2020) Synthesis of C11-to-C14 methyl-shifted all-trans-retinal analogues and their activities on human aldo-keto reductases. Org Biomol Chem 18:4788-4801.

Castellví A, Crespo I, Crosas E, Cámara-Artigas A, Gavira JA, Aranda MAG, Parés X, Farrés J, Juanhuix J (2019) Efficacy of aldose reductase inhibitors is affected by oxidative stress induced under X-ray irradiation. Sci Rep 9, 3177.

A new study from the ALBA Synchrotron explains the inefficacy of some diabetes drugs. UAB Divulga (2019) https://www.uab.cat/web/news-detail/a-new-study-from-the-alba-synchrotron-explains-the-inefficacy-of-some-diabetes-drugs-1345680342044.html?noticiaid=1345788995576

A new study from the ALBA Synchrotron explains the inefficacy of some diabetes discontinued drugs. News ALBA (2019) https://www.albasynchrotron.es/en/media/news/a-new-study-from-the-alba-synchrotron-explains-the-inefficacy-of-some-diabetes-drugs?set_language=en

Awarded the 2020 Xavier Solans Prize to Dr. Albert Castellví. https://www.ibmb.csic.es/en/news/awarded-the-2020-xavier-solans-award-to-dr-albert-castellvi/