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Discovering chemical solutions for neurodegeneration with the sweet molecules of life

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A lzheimer's disease (AD) is a fatal brain disease, whose etiology is still unknown. Treatment options are based mainly on inhibitors of both acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) enzymes. However, these therapeutics are not effective in preventing disease progression. AChE is the main enzyme responsible for the hydrolysis of the neurotransmitter acetylcholine. AChE activity decreases in specific brain regions as disease progresses, whereas BChE activity is upregulated, making it an attractive target for drug discovery. Abnormal expressions of BChE and AChE have also been observed in human tumors such as lung, colon and ovarian cancers. However, the relationship between altered enzyme expressions and tumorigenesis is not clear, nor is the efficacy of specific inhibitors as chemotherapeutic agents. We have disclosed a new family of highly selective and potent BChE inhibitors based on a purine nucleoside scaffold. In addition, we investigated the antitumor potential of such nucleosides on human lung and ovarian carcinomas, providing IC50 values with order of magnitude comparable to the chemotherapeutic cladribine. Furthermore, the induction of apoptosis was established and cell cycle analysis demonstrated a G2/M cell cycle arrest. These promising results encouraged us to develop new synthetic methodologies for the access to such molecules and to investigate the role of glycosyl structure and configuration in promoting activity as BChE selective inhibitor and anticancer agent. These results will be presented and discussed at the conference.

Biography

Amelia P Rauter has completed her PhD at the Technische Universität Graz, Institut für Organische Chemie in 1982 on the Chemistry of Glucuronolactone. She was the Founder of the Portuguese Chemical Society and Portuguese Carbohydrate Group, and the Founder and Leader of the Carbohydrate Chemistry Group at Faculdade de Ciências, Universidade de Lisboa. She is the Secretary of the European Carbohydrate Organisation and of IUPAC Division on Organic and Biomolecular Chemistry. She has been serving the Advisory Board of reputed journals and is the Editor of the Carbohydrate Chemistry: Chemical and Biological Approaches. Her research focuses on carbohydrate-based molecules efficient against diabetes and neurodegenerative diseases.

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