



Affichem S.A. is proud to announce that Dr. Marc POIROT will attend the 102nd Annual American Association for Cancer Research (AACR) Meeting on April 2-6 in Orlando, Florida, USA, where he will make an oral presentation entitled : “ **Discovery of Dendrogenin A as the first endogenous alkylaminooxysterol present in mammals with potent cell differentiation and anti-cancer activity** ”.

Abstract:

We recently reported that anti-tumor and chemopreventive drugs such as tamoxifen, raloxifene and docasahexaenoic acid are inhibitors at therapeutic doses of cholesterol epoxide hydrolase (ChEH), the enzyme that transforms cholesterol-5,6-epoxides (CE) into cholestane-3 β ,5 α ,6 β -triol (CT) (de Medina et al, *PNAS*, 2010). Several lines of evidence point to the existence of an active metabolism centered on CE. We recently reported that the aminolysis of α -CE by biogenic amines under catalytic conditions generated powerful cell differentiating alkylaminooxysterols (de Medina et al, *J Med Chem*, 2009). Among these active molecules, Dendrogenin A (DDA) was synthesized, based on the hypothesis that it could be an endogenous metabolite formed by the reaction of α -CE with histamine at the level of the ChEH. In the present study, we report the existence of DDA in mammals at concentrations ranging from 70 to 500 pmol/g in tissues and at concentrations 70 to 500 times less in the circulation, while only trace levels of AF17, the regio-isomer of DDA, were detected. DDA was not found in a panel of cancer cells, suggesting a possible deregulation of its synthesis during oncogenesis. In addition, we showed that DDA is the most potent natural inhibitor of ChEH with an IC50 around 100 nM and it exhibits tumor differentiation and anti-tumor activity in cell and animal models. *In vivo*, these effects were associated with a T cell-mediated anti-tumor response. AF17 was found to be inactive in these different tests, showing a regioselectivity of action of these compounds. In conclusion, our results shed light on a new metabolic pathway that generates the first endogenous steroidal alkaloid ever described in mammals that may have important functions in maintaining cell integrity and differentiation as well as immune system alert. The discovery of DDA reveals an unexpected cross-talk between cholesterol and histamine metabolism.

Author Block:

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Session Detail

Session Title: Steroid Receptors in Cancer Session

Type: Minisymposium

Session Start/End Time: Sunday, Apr 03, 2011, 3:15 PM - 5:15 PM

Location: Room W315, Orange County Convention Center

Session Category: Endocrinology 2

Session details : <http://www.abstractsonline.com/Plan/ViewSession.aspx?sKey=5c6cd159-d737-4a7d-8391-08d862575e83&mKey={507D311A-B6EC-436A-BD67-6D14ED39622C}>