



Séminaire Scientifique

Alexei Kisselev

Professeur de pharmacologie et de toxicologie

Department of Pharmacology and Toxicology, and Norris Cotton Cancer Center, Dartmouth Medical School, Lebanon/Hanover, New Hampshire, USA

« Development of specific inhibitors of proteasome active sites and their use to define distinct roles of these sites as drug targets in cancer »

Proteasomes degrade the majority of proteins in mammalian cells, are involved in the regulation of multiple physiological functions, and are established targets of anti-cancer drugs. The proteasome has three types of active sites: chymotrypsin-like, trypsin-like and caspase-like sites. All inhibitors used clinically were developed to block the chymotrypsin-like sites but they also co-inhibit other two sites. Whether inhibition of caspase- and/or trypsin-like sites is important for cytotoxicity was not clear. In order to answer this question we developed specific inhibitors of all three sites and demonstrated that inhibitors of caspase-like and trypsin-like sites sensitize malignant cells to inhibitors of chymotrypsin-like sites. Thus, trypsin-like and caspase-like sites have to be considered co-targets (with chymotrypsin-like sites) for anti-neoplastic agents; inhibition of two types of sites is needed to achieve maximal cytotoxicity of proteasome inhibitors.

Mardi 22 novembre 2011

11h00 au SIMOPRO (Saclay, Bât. 152)

En raison des conditions d'accès contrôlé au Centre d'Études de Saclay, les chercheurs français et étrangers qui désirent assister à ces conférences sont invités à contacter le secrétariat de l'iBiTec-S au moins une semaine avant la date de la conférence (Tél : 01.69.08.66.84, e-mail : celine.lentz@cea.fr). À la porte Nord (accès par la route D36), ces personnes devront présenter une pièce d'identité prouvant leur nationalité et devront préciser qu'elles viennent assister à la conférence de Biologie.

Due to the restricted access to the Centre d' Etudes of Saclay, foreign scientists who wish to attend these seminars should call the iBiTec-S office (Phone : 33.1.69.08.66.84, e-mail : celine.lentz@cea.fr) at least one week prior to the date of the conference. At the North entrance (D36 road), these scientists will have to present a passport to prove their nationality and state that they will attend the seminar of Biology.