DIPARTIMENTO DI FARMACIA E BIOTECNOLOGIE

Life & Chemical Sciences Seminars

DRUGGABLE TARGETS IN KEY SIGNALING PATHWAYS: PI3K/AKT AND BRAF/MEK SIGNALLING AND BEYOND

Dott.ssa Paola Perego

Molecular Pharmacology Unit, Dept. of Research Development and Applied Technologies, Fondazione IRCCS Istituto Nazionale dei Tumori di Milano

Mercoledì 14 marzo ore **10:00** – presso l' Aula A
ex-farmacologia via Irnerio 48
(ospite Prof. P. Romualdi)

Abstract

Survival of tumor cells is mediated by multiple networks including the PI3K/Akt and BRAF/MEK pathways. Experimental pharmacology efforts have led to the development of compounds capable to inhibit kinases acting on critical points of such pathways. Attempts to target these pathways have allowed the identification of drugs, which are under clinical investigation, or have been approved for treatment of specific diseases. Major efforts have been accomplished to hit the protein kinase Akt using small molecules that target the ATP binding domain or the pleckstrin homology (PH) domain. Besides, the BRAF/MEK signalling pathway has offered many chances for targeting the aggressive behaviour of tumor cells. Cellular pharmacology approaches have shown that direct targeting of survival pathways may result in an improvement of the efficacy of conventional antitumor agents. Efficient targeting of survival pathways may occur also by indirect approaches e.g., by epigenetic treatment using inhibitors of histone deacetylases (HDAC). Although many drugs targeting critical hubs of tumor cell survival pathways are already available, further efforts are required to identify compounds with improved pharmacological features and new agents targeting currently non-actionable mutations. Such a strategy will need resources to clarify the unknown biological significance of those alterations that are not druggable.

Biosketch

Education and training

1989-present, researcher in preclinical pharmacology (team leader from 2000) at Istituto Nazionale dei Tumori – Milan, Italy

1994-1996; Visiting Scientist at University of California, San Diego, UCSD Cancer Center, La Jolla, USA – Laboratory of Molecular Pharmacology

2009; Università degli Studi di Verona, PhD in Translational Biomedicine

1994; Università degli Studi di Milano, Diploma of Specialization in Applied Genetics

1989; Università degli Studi di Milano Degree in Biology (110/110 cum laude)

Involved in the preclinical development of conventional drugs and targeted agents. Interest in the overcoming of drug resistance with focus on various tumor types.

Selected publications

1. Gatti L. et al. New mechanisms for old drugs: insights into DNA unrelated effects of platinum compounds and drug resistance determinants. Drug Resistance Updates, 2015; 20:1-11.

2. Zuco V. et al. Targeting the invasive phenotype of cisplatin-resistant non-small lung cancer cells by a novel histone deacetylase inhibitor. Biochemical Pharmacology, 2015; 94 (2):79-90

3. Gatti L. et al. Histone deacetylase inhibitor-temozolomide co-treatment inhibits melanoma growth through suppression of Chemokine (C-C motif) ligand 2-driven signals. Oncotarget 2014; 5:4516-28

4 D'Arcy P et al. Inhibition of proteasome deubiquitinating activity as a new cancer therapy. Nat Med. 2011; 17:1636-40.

Commissione Ricerca e Attività Correlate