

REGULATION OF ION CHANNELS IN CARCINOGENESIS

PhD position (CNRS/PACA funding) available from September 2010 in the Institute of Developmental Biology and Cancer (UNSA CNRS UMR 6543), in the group of Dr Franck Borgese at the University of Nice Sophia Antipolis / CNRS, Nice, France.

Thesis supervisor: Dr Olivier Soriani

Our project will focus on the regulation of ion channels involved in cancer cell behaviour (apoptosis resistance, extra cellular matrix adhesion and degradation, motility, proliferation). Recently, we have demonstrated that a unique tumour biomarker, the sigma-1 receptor (Sig1R), was functionally associated to Cl⁻ and K⁺ channels in lung cancer and leukaemia cells. We have shown that the over-expression of Sig1R in cancer cells enhances cell apoptotic resistance through a decrease of volume-regulated Cl⁻ channels activation kinetics (Renaudo et al., 2007; Le Guennec et al., 2008). Moreover, exogenous sigma ligands inhibit cell cycle through a K⁺ channel / p27^{kip1}-dependent pathway (Renaudo et al. 2004).

The project will deal on the molecular mechanisms associating the Sig1R to ion channels aberrantly expressed in leukaemia and breast cancer cells, in relation to their aggressiveness state. Finally, *in vivo* significance of the described mechanisms will be explored in a mouse metastatic model.

Main technical approaches: Molecular cell biology, genetics, microscopy imagery and electrophysiology (patch-clamp).

We are seeking highly talented and self-motivated candidates. A background in the field of electrophysiology and cell physiology will be appreciated. The position will be available on September 2010.

Candidates are invited to obtain application forms from soriani@unice.fr or borgese@unice.fr
Application deadline: Friday 30th April.

Provisional date for auditions of short listed candidates: Monday 17th May

Références:

- Martial,S., Giorgelli,J.L., Renaudo,A., Derijard,B., and Soriani,O. (2008). SP600125 inhibits Kv channels through a JNK-independent pathway in cancer cells. *Biochem. Biophys. Res. Commun.* 366, 944-950
- Renaudo,A., L'Hoste,S., Guizouarn,H., Borgese,F., and Soriani,O. (2007). Cancer cell cycle modulated by a functional coupling between sigma receptors and Cl⁻ channels. *J. Biol. Chem.* 282, 2259-2267.
- Le Guennec,J.Y., Ouadid-Ahidouch,H., Soriani,O., Besson,P., Ahidouch,A., and Vandier,C. (2007). Voltage-gated ion channels, new targets in anti-cancer research. *Recent Patents Anticancer Drug Discov.* 2, 189-202.
- Renaudo,A., Watry,V., Chassot,A.A., Ponzio,G., Ehrenfeld,J., and Soriani,O. (2004). Inhibition of tumor cell proliferation by sigma ligands is associated with K⁺ Channel inhibition and p27^{kip1} accumulation. *J. Pharmacol. Exp. Ther.* 311, 1105-1114.