institut Valrose
Biologie

A two year post-doctoral position in Neurobiology will be available (September) at the "Institut de Biologie Valrose" (iBV) located in Nice, France. The Institute of Biology Valrose (http://ibv.unice.fr/EN/index.php) is one of France's premier life science research centers and offers an international scientific environment with 250 persons working in 20 research groups. The project will be carried out in the ATIP-Avenir group " Biology of ion channels" to investigate the role of K_{2P} potassium channels using new optogenetic approaches.

Ion channels generate the electrical signals with which the nervous system senses the world, processes information, creates memories and controls behavior. One of the most diverse families of ion channels, the K_{2P} channels, serves as a hub for the generation and regulation of the negative resting membrane potential and neuronal excitability. K_{2P} TREK1 channels also play a central role in the response of cells to extracellular and intracellular signals as diverse as GPCR signaling, pH, membrane stretch and pharmacological agents such as fluoxetine. TREK1 channels have been shown to be involved in many physiological functions such as neuroprotection afforded by PUFAs against ischemia and depression. These properties of TREK1 suggest it as an attractive pharmacological target for the development of new drugs and provide motivation for a deeper understanding of this channel's function. However, the absence of specific pharmacology renders functional and structural studies of K_{2P} TREK1 channels difficult. To overcome this limitation, we recently developed a TREK1 channel that can be controlled by light *via* a tethered photoisomerizable pore blocker. This photoswitchable channel, called TREKlight, behaves like wild-type channel in visible light but a pulse of UV light reversibly closes it. To address the role of TREK1, we adapted TREKlight to develop "photoswitchable conditional subunit" (PCS-TREK1) form of TREK1 which allows natively expressed channels to be targeted and reversibly regulated by light *in vitro* and *ex vivo*. Currently, we are also developing the "StarTREK" mouse. The StarTREK mouse model has the WT-TREK1 channel gene replaced by TREKlight. Since TREKlight has the same properties as WT-TREK1, this mouse will be identical to a WT-mouse. But this mouse will allow us to address, *in vivo*, the function of TREK by having the ability to control the channel activity with light.
The candidate will work on two aspects:

(i) At the fundamental level: the applicant will study the TREK channel function using light with the TREK1-PCS strategy and the StarTREK mice.
(ii) At the technical level: the applicant will develop new optical tools to endow optical control of other multi-subunit signaling proteins.

The ideal candidates will have a solid background in electrophysiology (slice-patching experience would be appreciated) and molecular biology and/or cell imaging and/or optogenetic.

Interested candidates should e-mail a letter of application, including a CV and the names and addresses of at least two referees to: Guillaume Sandoz, sandoz@unice.fr.

Ref:

Sandoz G**,** Levitz J, Kramer R & Isacoff EY. (2012) *Optical control of endogenous proteins with a photo-switchable conditional subunit reveals a role for TREK1 in GABAB signaling*. **Neuron**, 74; 1005-14.

Janovjak H*, Sandoz G* & Isacoff EY. (2011). A modern ionotropic glutamate receptor with a K+ selectivity signature sequence. **Nature Communications**, 2:232

Sandoz, G., Bell S.C., and Isacoff EY. (2011). Optical probing of a dynamic membrane interaction that regulates the TREK1 channel. 2011, **Proc Natl Acad Sci U S A** 8;108(6):2605-10

Sandoz G, Douguet D, Chatelain F, Lazdunski M, Lesage F. (2009). Extracellular acidification exerts opposite actions on TREK1 and TREK2 potassium channels via a single conserved histidine residue. 2009, **Proc Natl Acad Sci U S A** 106:14628-33.

Sandoz G**,** Tardy M, Thümmler S, Feliciangeli S, Lazdunski M & Lesage F, *Mtap2 is a constituent of the protein network that regulates TREK channel expression and trafficking.* **Journal of Neuroscience,** 28, 8545-8552.