

# Newsletter

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## Peptide meeting at the University of Rouen

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**THEMATIC DAY**

**PEPTIDE DELIVERY FOR THERAPEUTIC AND COSMETIC APPLICATIONS**

MAISON DE L'UNIVERSITÉ  
UNIVERSITY OF ROUEN  
MONT-SAINT-AIGNAN CAMPUS  
26<sup>th</sup> NOVEMBER 2014  
9AM-5PM

**GUEST SPEAKERS**  
IJEOMA UCHEGBU (NANOMERICS)  
JOEL RICHARD (IPSEN)  
MICHEL KHRESTCHATISKY (VECT-HORUS)  
PAOLO BOTTI (ARISGEN)  
KARL LINTNER (KAL'IDÉES)

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Registration and abstract submission:

Researchers from the University of Rouen, in partnership with Cosmetic Valley cluster, Technopole CBS and GFPP, will organize a series of lectures on "Peptide delivery for therapeutic and cosmetic applications" at the Maison de l'Université, on the campus of Mont-Saint-Aignan, University of Rouen, on November 26, 2014. This meeting will bring together international experts including **Ijeoma UCHEGBU** (Nanomerics), **Paolo BOTTI** (Arisgen), **Michel KHRESTCHATISKY** (Vect-Horus), **Joel RICHARD** (Ipsen) and **Karl LINTNER** (KAL'Idées). Oral presentations will be selected from submitted abstracts. Participation to this event is free but registration is mandatory at the following address: <http://primacen.fr/Event/?id=Mw>. For further information, please contact **David VAUDRY** ([david.vaudry@univ-rouen.fr](mailto:david.vaudry@univ-rouen.fr)) or **Jerome LEPRINCE** ([jerome.leprince@univ-rouen.fr](mailto:jerome.leprince@univ-rouen.fr)).

## 19<sup>th</sup> GFPP Congress

The 19th GFPP congress (French Group of Peptides and Proteins) will take place in Portbail (Manche) from May 17 to 22, 2015. More than 200 scientists working in the field of peptides and proteins will present their work in a unique environment combining scientific sessions and accommodation, to foster collaborations. This conference will give doctoral and post-doctoral students the opportunity to meet with French and foreign top-level researchers through thirty reserved scholarships. For further information visit: [www.gfpp.fr](http://www.gfpp.fr).



## PeReNE at RICT 2014



The 50th International Conference on Medicinal Chemistry (RICT 2014) was held in Rouen from July 2 to 4, 2014. The conference was attended by nearly 600 scientists, academics and manufacturers around the theme "Interfacing Chemical Biology and Drug Discovery." Over 25 plenary lectures were given, many of which highlighted the potential of peptides and peptidomimetics in the discovery of new drugs. The PeReNE project sponsored this conference and promoted the skills of the project network's teams and Platforms.

## Science Festival 2014

The PERENE project will be hosted at the Science Village at the Technopôle du Madrillet in Saint-Etienne du Rouvray, during the Science Festival, from October 9 to 11, 2014. Activities introducing peptides for school children will be offered. For further information, contact **Magalie BÉNARD** ([magalie.benard@univ-rouen.fr](mailto:magalie.benard@univ-rouen.fr)).



## 4<sup>th</sup> PeReNE Steering Committee



The fourth Steering Committee for the PERENE project will be organized by **Michèle BOITEL**, **Francois GUÉRINEAU** and colleagues from the University of Picardie Jules Verne in Amiens, on October 27-28, 2014. This committee will gather French and English team members of the PERENE Network, in order to take stock of the activities during the year 2014 and prepare the final conference and project closure. Scientific conferences as well as poster communications will present the latest results of the ongoing projects.



## Recruitment

**Marine LE MERCIER** joined INSERM U982 to animate the PERENE project after **Paul GIULIANI**'s departure. She will take over the administrative and financial management for the PERENE project, as well as organize the various events and communication activities of the project.

## Conferences

During the 20th International Symposium on Regulatory Peptides to be held in Kyoto from September 7 to 10, 2014, Dr. **David VAUDRY** will give a lecture entitled "*Characterization of PACAP neuroprotective effects and approaches for therapeutic applications.*" At the same meeting Dr. **Hélène CASTEL** will give a talk entitled "*The vasoactive peptide urotensin II: a new chemokine exhibiting migration / adhesion properties in glioma.*"

## Are urotensinergic peptide ligands new chemokines? Roles in neo-angiogenic and invasive processes of brain glioma tumors

**Pierre-Olivier Guichet, Vadim Le Joncour, Céline Lecointre, Laurence Desrues, Nicolas Perzo, Marie-Christine Tonon, Fabrice Morin, François Proust, Pierrick Gandolfo and Hélène Castel**

*U982 Inserm, Laboratoire de Communication et Différenciation Neuronale et Neuroendocrine, DC2N, IRIB, PeReNE network, Université de Rouen, France*

Gliomas are the most common form of primary tumors of the central nervous system. The most aggressive glioma, the multiform glioblastoma (GBM), is particularly resistant to chemo/radiotherapy, and relapse is almost systematic. Despite significant therapeutic and conceptual advances, there is currently no curative treatment, hence a median survival expectancy of 15 months. Future therapies must take into account the invasion of healthy tissue which occurs in response to chemoattractant factors including vasoactive peptides capable of activating G protein-coupled receptors (GPCR). The « Astrocyte and Vascular Niche » team at INSERM U982 is interested in the vasoactive peptide urotensin II (Ull) receptor, the UT receptor, a chemoattractant receptor similar to the CXCR4 receptor.

Previous studies had revealed the presence of mRNA encoding the receptor of the Ull peptide and protein in cortical astrocytes in rat, in culture<sup>1-3</sup> and in the U87<sup>3</sup> glioblastoma line. The peptide and its receptor are indeed expressed in many tumor types including GBM<sup>4</sup> lines. Recent work by the team shows, from a histopathological study of 50 gliomas (collaboration Prof A. Laquerrière, CHU Rouen), higher expression of the couple Ull/UT in astrocytomas compared with oligodendrogliomas. Furthermore, a strong discrete expression is observed in peri-vascular and peri-necrotic areas in GBM. Finally, the higher expression in grade III and IV shows that there is a correlation with tumor grade.

*In vitro*, exposure to a gradient of Ull concentration induces the migration of GBM cell lines primarily through the recruitment of the G<sub>α13</sub> protein and the activation of the signaling pathway Rho/ROCK. Conversely, a homogeneous concentration of ligand inhibits cellular motility and favors adhesion through the recruitment of the G<sub>αi/o</sub> protein and activation of the PI3K pathway. These results show the role of UT as chemotactic receptor relaying signaling changes depending on the Ull ligand concentrations. *In vivo*, our studies show that Ull accelerates tumor growth with attraction of macrophages, neovascularization and necrosis in a heterotopic xenograft model of U87 cells in Nude mice. We believe that our analysis of the "biased" character of some urotensinergic ligands will make their use in a therapeutic perspective possible<sup>5</sup>.

- 1 Castel, H., Diallo, M., Chatenet, D., Leprince, J., Desrues, L., Schouft, M.-T., Fontaine, M., Dubessy, C., Lihmann, I., Scalbert, E., Malagon, M., Vaudry, H., Tonon, M.-C., and Gandolfo, P. (2006) Biochemical and functional characterization of high-affinity urotensin II receptors in rat cortical astrocytes. *J. Neurochem.*, 99, 582–595.
- 2 Jarry, M., Diallo, M., Lecointre, C., Desrues, L., Tokay, T., Chatenet, D., Leprince, J., Rossi, O., Vaudry, H., Tonon, M.-C., Prézeau, L., Castel, H., and Gandolfo, P. (2010) The vasoactive peptides urotensin II and urotensin II-related peptide regulate astrocyte activity through common and distinct mechanisms: involvement in cell proliferation. *Biochem. J.*, 428, 113–124.
- 3 Desrues, L., Lefebvre, T., Lecointre, C., Schouft, M.-T., Leprince, J., Compère, V., Morin, F., Proust, F., Gandolfo, P., Tonon, M.-C., and Castel, H. (2012) Down-regulation of GABA(A) receptor via promiscuity with the vasoactive peptide urotensin II receptor. Potential involvement in astrocyte plasticity. *Plos One*, 7, e36319.
- 4 Takahashi, K., Totsune, K., Murakami, O., and Shibahara, S. (2001) Expression of urotensin II and urotensin II receptor mRNAs in various human tumor cell lines and secretion of urotensin II-like immunoreactivity by SW-13 adrenocortical carcinoma cells. *Peptides*, 22, 1175–1179.
- 5 Perzo N., Brulé, C., Joubert JE., Sainsily X., Leduc R., Prézeau L and Castel H.. Biased signaling regulates the pleiotropic effects of the urotensin II receptor to modulates its cellular behaviors. *Faseb J*, In press.