BORDEAUX RNA Club

Thursday September 26th, 2013

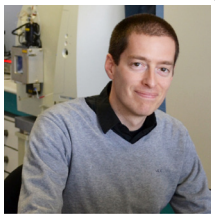
At the European Institute of Chemistry and Biology

14.00 ***ARNm dendritiques et axonaux, et leur rôle dans le développement, la plasticité et la physiologie du système olfactif de la souris.***

Pr. Alain Trembleau, Université Pierre et Marie Curie, Paris, France

Abstract: Le système olfactif de la souris se construit selon un schéma de développement extrêmement complexe, qui se poursuit tout au long de la vie de l'animal en raison de processus de neurogénèse continue des populations de neurones sensoriels et d'interneurones centraux. Dans les neurones sensoriels olfactifs les ARNm codant les récepteurs de molécules odorantes sont localisés non seulement dans le corps cellulaire mais également dans le compartiment axonal. Dans les interneurones du bulbe olfactif, la protéine de liaison aux ARN FMRP (Fragile X Mental Retardation Protein) est présente dans le compartiment dendritique, avec certains de ses ARNm cibles. Au cours de mon exposé, je présenterai les approches que nous avons développées pour analyser les mécanismes moléculaires et cellulaires du transport et de la traduction locale de ces ARNm, ainsi que leur fonction dans ces compartiments neuronaux.

15.00 ***Mass Spectrometry of nucleic acids. Current state of MS-based approaches devised to overcome the limitations of traditional techniques.***



Dr. Frédéric Rosu, Institut Européen de Chimie et de Biologie, Bordeaux, France

Abstract : We will explore in a brief overview how MS-based approaches can reach well beyond sequence information to provide correlations between sequence, higher-order structure, and relationships with other cellular components, which are necessary to understand nucleic acids function and mechanism of activity. We will also discuss newly advanced techniques in mass spectrometry like ion spectroscopy and top-down mass spectrometry applied to nucleic acids. .

15.30 ***Amphiphile oligonucleotides – agonists of TLR7***

Nataliia Beztsinna, PhD Student, Université de Bordeaux, France

Abstract : N. Beztsinna, J.-Ph. Heurbeuval, I. Bestel

Toll-like receptors recognize pathogen-associated molecular patterns and elicit pathogen-specific innate and adaptive immune responses. Of the 11 TLRs identified in humans, TLR3, 7, 8 and 9 are expressed in endolysosomes and recognize pathogen-derived and synthetic nucleic acids. TLR7 is exclusively expressed in plasmacytoid dendritic cells and its stimulation by viral RNAs leads to massive secretion of IFN α and other proinflammatory cytokines. Agonists of TLR7 are therefore of major interest for the immunotherapy in general and especially in cancer. Existing TLR7 agonists are represented by two groups: small molecules (ex. Imiquimod) and synthetic single stranded RNAs. Imiquimod and its analogues are already used in clinic for the topical treatment of skin neoplasias; however they are not suitable for systemic administration. ssRNA could be a promising alternative but they suffer from poor cellular uptake and short residence time in biological medium. In our laboratory we developed amphiphile olinucleotides (ONs) – synthetic bioconjugates between RNA or DNA strand and a lipid chain. It was shown that these molecules are able to enter cancer cells without transfection reagents and accumulate in endosomal compartments. We've decided to use this strategy to conceive new agonists of TLR7. Moreover the presence of lipid issued from viral envelope could increase TLRs stimulation. Firstly we synthesized, purified and analyzed a small library of 13 ONs. Amphiphile bioconjugates were prepared by automatic oligonucleotide synthesis or post-synthetically by a click chemistry reaction. The library was evaluated by a stimulation test on human pDCs derived from heath donors. Surprisingly we found that depending on their lipid chain the prepared molecules activate different pathways in pDCs. These preliminary results helped us to identify the most promising candidates for further investigations.

16.00 ***Using NMR spectroscopy to study G-quadruplex nucleic acids inside living cells***

Dr. Gilmar Salgado, Laboratoire ARNA, INSERM U869, Bordeaux, France

Abstract : G-quadruplexes are unusual three dimensional structures of nucleic acids, which have recently started to be used as targets for novel ligands with anticancer properties. A major problem in designing new ligands, is to obtain precise and selective structural information concerning the «receptor» ligand complex, preferable from inside living cells. In this study we show that after exposing the cells with an extracellularly administered G-quadruplex ligand, that it is possible to follow modifications in the conformation of the G-quadruplex inside cells.

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