EAS-0335.
ANGIOGENESIS POTENTIALIZED BY HIGHLY SULFATED FUCOIDAN: ROLE OF THE CHEMOKINES AND THE PROTEOGLYCANS

N. Marinval*, P. Sabboural, O. Haddad, D. Letourneur, N. Charnaux, H. Hlawaty. *Laboratory for Vascular Translational Science, Inserm, Paris, France*

* Corresponding author.

Low molecular weight fucoidans (LMWF) are natural sulfated polysaccharides used as glycosaminoglycans (GAG) mimetics. Both GAGs and chemokines are important to regulate angiogenesis and wound healing. LMWF interacts with chemokines, such as RANTES/CCL5 and SDF-1/CXCL12, leads to re-endothelialization (Yangguang *et al.*, 2010) and increases endothelial cell migration (Hlawaty *et al.*, 2011). However the pro-angiogenic activity of LMWF still remains unclear and depends of the type of fucoidan. Innovative vascular therapies based on natural GAG mimetic should be developed.

In order to understand the beneficial action of LMWF on vascular regeneration and angiogenesis we propose to analyze fucoidan's structure-function relationships. We hypothesize that the size and sulfation level could regulate the chemokines affinity and modulate its beneficial properties.
We purified and characterized 5 fractions of LMWF according to their sulfation rate. We tested their affinity to chemokines (Surface Plasmon Resonance), the effect on endothelial cells (HUVEC) migration (Boyden chamber) and their pro-angiogenic properties (Microvascular tube formation). We also analyzed the effect of fucoidans on endogen GAG expression (qRT-PCR, FACS).
The structural analysis of fucoidans resulted in fractions (5-27kDa) composed of fucose, sulfate and uronic acid. The most sulfated LMWF fraction (5kDa with ratio sulfate/fucose at 1.87) presented high affinity to biotinylated-SDF-1/CXCL12 and RANTES/CCL5. Moreover, 5kDa LMWF significantly increased HUVEC migration and vascular network formation compared to other LMWF fractions.
The 5 kDa LMWF shows the highest pro-angiogenic effects on HUVEC. Fucose-Sulfate-Rich 5kDa LMWF confirmed our hypothesis than small and highly sulfated fucoidan is attractive candidate to develop therapies based on revascularization.

EAS-0666.
EFFECT OF N-ACETYLCYSTEINE INDICATORS OF PROINFLAMMATORY CYTOKINES IN PATIENTS WITH ACUTE CORONARY SYNDROME WITH ST SEGMENT ELEVATION

A. Nizomov*. *Cardilogy, Hospital National Holding Company "UZBEKNEFTEGAS", Tashkent, Uzbekistan*

* Corresponding author.

Ischemia following acute coronary syndrome with ST segment elevation (ACS) increases the level of pro-fibrotic and inflammatory cytokines, including transforming interleukin 6 (IL6) and tumor necrosis factor (TNF)-α. N-acetylcysteine (NAC) has therapeutic benefits in the management of patients with ACS. To the best of our knowledge, this is the first study that has evaluated the effect of NAC on TNF-α and IL6 levels in patients with ACS.

Methods: Following confirmation of ACS, 88 patients were randomly administered NAC 600 mg or placebo orally twice daily for 3 days. For quantification of IL6 and TNF-α serum levels after 24 and 72 h of NAC or placebo administration, peripheral venous blood (10 mL) samples were collected at these time points.
Results: Comparisons between levels of IL6 and TNF-α after 24 and 72 h within the NAC or placebo groups revealed that there was not any significant difference except for IL6 levels in the placebo group, which increased significantly over time ($p = 0.042$). Significant relationships existed between patients' ejection fraction ($p = 0.005$) and IL6 levels.
Conclusions: Receiving NAC could prevent IL6 levels from increasing after 72 h as compared with not receiving NAC. As IL6 had strong correlations with the ejection fraction, its antagonism seems to be important in the prevention of remodeling.

EAS-0672.
TARGETED LIPOSOMAL DRUG DELIVERY TO INHIBIT ATHEROSCLEROTIC PLAQUE INFLAMMATION

A. Alaarg[1,*], A.A.J. Hamers[2], M. Versloot[2], M.E. Lobatto[3], W.J.M. Mulder[4], E.S.G. Stroes[3], G. Storm[5], J.M. Metselaar[1]. [1] *Targeted Therapeutics section-Department of Biomaterials Science and Technology-MIRA Institute, University of Twente, Enschede, Netherlands;* [2] *Department of Experimental Vascular medicine, Academic Medical Centre, Amsterdam, Netherlands;* [3] *Department of Vascular Medicine, Academic Medical Centre, Amsterdam, Netherlands;* [4] *Translational and Molecular Imaging Institute, Mount Sinai School of Medicine, New York, USA;* [5] *Department of Pharmaceutics-Utrecht Institute for Pharmaceutical Sciences (UIPS), Utrecht University, Utrecht, Netherlands*

* Corresponding author.

Atherosclerosis is a chronic, lipid-driven inflammatory disease. Encapsulation of drugs into nanocarriers such as liposomes can improve the pharmacokinetic profile of the drug and enhance its bioavailability to the atherosclerotic plaque, thereby improving the therapeutic efficacy of the drug and minimizing its side effects. Macrophages are crucial in the development and progression of atherosclerosis. We showed that liposomes can target the atherosclerotic plaques in LDL-r KO mice and can be engulfed by macrophages. To determine which compounds is to be encapsulated into liposomes, we selected compounds that can tackle the most relevant pathophysiological pathways in atherosclerosis in which macrophages play a key role: inflammation, oxidative stress, proliferation and oxidized lipid handling. We set up a battery of in vitro assays to assess the effect of the selected compounds in human and murine macrophages under conditions that imitate the atherosclerosis milieu. Prednisolone, the liver X receptor (LXR) agonist T09, Simvastatin and Pterostilbene significantly inhibited NF-κB activity. On the axis of lipid handling, T09, Pterostilbene and Simvastatin supressed the uptake of oxidized low density lipoprotein (ox-LDL). Using BRdU labelling, we also demonstrate that Pterostilbene and Simvastatin suppressed the proliferation of macrophage. T09 and Pterostilbene showed anti-oxidant activities in the oxidative burst assay. We conclude that Pterostilbene, Simvastatin and T09 are potential candidates for targeted delivery to the atherosclerotic plaques.

EAS-0939.
REVERSING ATHEROSCLEROSIS NATURALLY: ANTIOXIDANT AND POTENTIAL ANTI-INFLAMMATORY ACTIVITY OF GARCINIA MANGOSTANA

S. Reverentia[1,*], D. Djunaedi[2], D. Sargowo[3]. [1] *Cardiology dan Vascular Medicine, Institute of Molecular Biology of Malang, Malang, Indonesia;* [2] *Internal Medicine, Faculty of Medicine University of Muhammadiyah Malang, Malang, Indonesia;* [3] *Cardiology and Vascular Medicine, Brawijaya Medical School / Dr. Saiful Anwar General Hospital, Malang, Indonesia*

* Corresponding author.

Background: Atherosclerosis, formerly considered a bland lipid storage disease, actually involves an ongoing inflammatory response. Recent advances in basic science have established a fundamental role for inflammation in mediating all stages of this disease from initiation through progression and, ultimately, the thrombotic complications of atherosclerosis. Thus, we believe that inflammatory processes may be potential targets of therapy in preventing or treating atherosclerosis and its complications.

Aims: This present study highlights antioxidative and anti-inflammatory activities of xanthones from pericarp of *Garcinia mangostana* ethanol extract in experimentally induced atherosclerotic rats.
Methods: 30 albino rats were divided into five experimental groups of six animals. One group remained as distilled water treated control and other four groups were experimentally induced atherosclerotic rats. Crude ethanol extract were prepared and given orally to three groups at 200 mg/kgBW, 400 mg/kgBW and 800 mg/kgBW for 90 days and the other remained untreated control. Blood samples were collected at the end of experiment (90 days) for measurement of Tumor necrotic factor-α (TNF-α)