Up to two Postdoctoral Fellows:
Assessment of a new therapeutic class for dyslipidemia & cardiovascular diseases.

Description of the institute of metabolic and cardiovascular diseases (I2MC)

The I2MC (http://www.i2mc.inserm.fr) is one of the larger institute in France dedicated to metabolic and cardiovascular diseases. The main feature of I2MC is the gathering of basic scientists together with clinicians working on metabolic risk factors (obesity, diabetes and dyslipidemia) and their cardiovascular complications (thrombosis, atherosclerosis, cardiac and renal failure). I2MC is composed of 13 research teams. The research of team wherein the post-doc is proposed, directed by Laurent Martinez, is focused on the metabolic and vascular atheroprotective functions of High Density Lipoproteins (HDL), from molecular, cellular and preclinical research to clinical investigations in human cohorts.

Job description

Background. Cardiovascular diseases (CVD) are one of the main causes of mortality worldwide. The protective effect of HDL-cholesterol (HDL-C) in cardiovascular disease is supported by many epidemiological studies and is now widely accepted. Indeed, HDL has the unique ability to excreted cholesterol excess out of the body through uptake by the liver for subsequent excretion into the bile. In addition, HDL exerts direct vascular beneficial functions by protecting coronary arteries. Statins are first-line therapy for the treatment of dyslipidemia because of their LDL-C lowering efficacy. However, even in high-risk patients treated to aggressive LDL-C goals, coronary events still occur at a high rate and low HDL-C is a major risk factor. Thus, a natural next step in the search for therapies to reduce cardiovascular morbidity and mortality further involves raising HDL-C levels and/or improving HDL particles quality and functions. One HDL-C raising drugs has recently shown to significantly reduce major coronary events compared to placebo in patients at risk for cardiac events (REVEAL study). This open up new therapeutic perspectives for the development of combined therapies aiming to raise HDL-C AND improve HDL functional state with their beneficial properties for cardiovascular health.

Duties. The applicant will be expected to conduced pre-clinical research aiming to evaluate the effect of a new therapeutic class of molecules improving the functional state of lipoproteins. This will include to evaluate their acute and chronic efficacy on preclinical models of dyslipidaemia and atherosclerosis. Pharmacological studies (PK/PD, ADME, Tox, TK, immunoTox…) and lead optimization will be also performed through an industrial partnership and subcontracting. Beyond therapeutic efficacy, the molecular mechanisms involved will be also investigated. Theranostic biomarkers will be also evaluated on different cohorts.

Entry requirement. The work will involve *in vivo* studies. For one of the positions, the candidate must have a proven experience and knowledge in experimental models of atherosclerosis, cardiac dysfunction and/or lipid metabolism disorders. For the other position, experience in cell signaling, intracellular trafficking and molecular biology is required. Candidates should ideally have broad knowledge of science, and experience in the fields of vascular biology, lipid/lipoprotein metabolism, biochemistry, and pharmacology. Additional experience with the following technologies should be considered a plus: experience with human samples and biobanks, bioinformatics, and functional immune assays. He/she is expected to cooperate in national and international networks (academic & CRO), so experience of working in networks of researchers and English language skills at a high level is required. International research experience gives an extra value. The scientific breadth of the employment requires good cooperation and communication skills. The applicant must be organized, thorough, proactive and a talented problem solver.

Funding. Salary and project are guaranteed by multiple funding (French National Research Agency, the Occitania region and private funds). The position is for 18-months and the candidate can start as soon as January 1st, 2018. Salary is highly attractive and will depend on the candidate's experience.

Application procedure

Interested applicants should submit a motivation letter, a curriculum vitae including a full list of publications and at least two references to laurent.martinez@inserm.fr. Submissions should include the mailing label "Post-doctoral position CVD".

Major publications of the team

Genoux A, Lichtenstein L, Ferrières J, Duparc T, Bongard V, Vervueren PL, Combes G, Taraszkiewicz D, Elbaz M, Galinier M, Nassar B, Ruidavets JB, Perret B, Martinez LO. Serum levels of mitochondrial inhibitory factor 1 are independently associated with long-term prognosis in coronary artery disease: the GENES Study. BMC Med. 2016 Aug 23;14(1):125.

Lichtenstein L, Serhan N, Espinosa-Delgado S, Fabre A, Annema W, Tietge UJ, Robaye B, Boeynaems JM, Laffargue M, Perret B, Martinez LO. Increased atherosclerosis in P2Y13/apolipoprotein E double-knockout mice: contribution of P2Y13 to reverse cholesterol transport. Cardiovasc Res. 2015 May 1;106(2):314-23.

Fabre AC, Malaval C, Ben Addi A, Verdier C, Pons V, Serhan N, Lichtenstein L, Combes G, Huby T, Briand F, Collet X, Nijstad N, Tietge UJ, Robaye B, Perret B, Boeynaems JM, Martinez LO. P2Y13 receptor is critical for reverse cholesterol transport. Hepatology. 2010 Oct;52(4):1477-83.

Martinez LO, Jacquet S, Esteve JP, Rolland C, Cabezón E, Champagne E, Pineau T, Georgeaud V, Walker JE, Tercé F, Collet X, Perret B, Barbaras R. Ectopic beta-chain of ATP synthase is an apolipoprotein A-I receptor in hepatic HDL endocytosis. Nature. 2003 Jan 2;421(6918):75-9.