

Activités scientifiques

Summary

The research activities of the group centres on the role of high density lipoproteins (HDL) in cardio-protection. Their protective role appears to be compromised in diabetic patients, where serum concentrations are significantly reduced compared to non-diabetic subjects. Our particular interest are the factors and mechanisms by which HDL are protective. We have two objectives. One series of studies is investigating the anti-oxidant function of HDL. They focus on an enzyme associated with HDL, termed paraoxonase. Its anti-oxidant role is well established, and it has been shown to be an independent risk factor for vascular disease. Its activity is lower in diabetic patients. The second objective is a direct effect of HDL on the heart. Our studies have shown that HDL can reduce the consequences of ischemia-reperfusion injury, which is a major problem during re-vascularisation after a myocardial infarction. Using *in vitro*, *ex vivo* and *in vivo* models, we have demonstrated that HDL can reduce the size of the infarct area, limiting damage to heart function and future risk of heart failure. One particular component of HDL, the lipid sphingosine-1-phosphate appears essential for the protective effect of HDL. The molecular mechanisms underlying the effect of HDL in cardiomyocytes is also being investigated.

Publications :

1. Frias, M.A., Lecour, S., James, R.W. and Pedretti, S. (2012)
High density lipoprotein/sphingosine-1-phosphate-induced cardioprotection. Role of STAT3 as part of the SAFE pathway.
JAK-STAT 1, 1–9.
2. Ancrenaz, V., Desmeules, J., James, R., Fontana, P., Reny, J-L., Dayer, P. and Daali, Y. (2012)
Paraoxonase-1 pathway is not a major bioactivation pathway of clopidogrel *in vitro*.
British J Pharmacol 166, 2362-70.
3. Costanza, M.C., Beer-Borst, S., James, R.W., Gaspoz, J.M. and Morabia, A. (2012)
Consistency between cross-sectional and longitudinal SNP: blood lipid associations.
Eur J Epidemiol 27, 131-8.
4. Pétremand, J., Puyal, J., Chatton, J-Y., Duprez, J Allagnat, F., Frias, M., James, R.W., Waeber, G., Jonas, J-C. and Widmann, C. (2012)
HDLs protect pancreatic beta cells against ER stress by restoring protein folding and trafficking.
Diabetes 61, 1100-11.
5. Pfenniger, A, Foglia, B., Dunoyer-Geindre, S., Haefliger, J-A., Winnik, S., Mach, F., James, R.W. and Kwak, B.R. (2012)
Lack of association between connexin40 polymorphisms and coronary artery disease.
Atherosclerosis 222, 148-53.
6. Rossier, M.F., Pagano, S., Python, M., Maturana, A.D., James, R.W., Mach, F., Roux-Lombard, P. and Vuilleumier, N. (2012)

Anti-apolipoprotein A-1 IgG chronotropic effects require non genomic action of aldosterone on L-type calcium channels.
Endocrinology 153, 1269-78.

7. Morel, S., Frias, M.A., Rosker, C., James, R.W., Rohr, S. and Kwak, B. R. (2012)
The natural cardioprotective particle HDL modulates connexin43 gap junction channels.
Cardiovasc Res 93, 41-9

8. James, R.W, Frias, M. and Lecour, S. (2012)
Lipid-induced modulation of protective signalling pathways in cardiovascular disease.
Curr Signal Trans Therapy 7, 96-103.