Inserm
Délégation régionale
Midi-Pyrénées, Limousin

UMR 1048 (I2MC)
Equipe 9

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Athérothrombose : rôle des oestrogènes, nouvelles approches thérapeutiques

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Cette équipe de recherche fait partie de l'unité Inserm 1048, mixte avec l'Université de Toulouse III (I2MC ou Institut des maladies métaboliques et cardiovasculaires).

Objectif scientifique

In the last years, our group contributed to evidence that, beside the prevention of osteoporosis, targeting estrogen signalling represents an attractive and effective perspective to prevent the development or the progression of atherosclerosis as well as type 2 diabetes.
We demonstrated that ERalpha, but not ERbeta is absolutely necessary for the vasculoprotective effects of E2 in atheroma, NO production and reendothelialization, as well as on insulin sensitivity and glucose tolerance.
In face to these numerous beneficial cardiovascular and metabolic actions, the dark side of estrogens is represented by their deleterious long-term action on one of their main sexual target, the mammary gland, and the promotion of breast cancer.
We demonstrated recently that ERalpha AF-1 is not required for three major vasculoprotective actions of E2, whereas it is necessary for the effects of E2 on its reproductive targets. Thus, we demonstrated the possibility to uncouple the beneficial vascular actions from the sexual actions, and thereby the molecular rationale to develop selective ER modulators with an attractive profile in preventive medicine. Thus, we demonstrated the possibility to uncouple the beneficial vascular actions from the sexual actions, and thereby the molecular rationale to develop selective ER modulators with an attractive profile in preventive medicine. Our final goal is to open new perspectives regarding the modulation of ERα by phytoestrogens / Selective Estrogen Receptor Modulator (SERM), providing the rationale to select and/or develop, among molecules eliciting minor sexual actions (i.e. minor AF-1 activation), those activating preferentially AF-2 and/or MISS and, thereby, having also beneficial effects in the prevention of cardiovascular and metabolic diseases.

Retombées attendues en santé

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Mots clés

Athérome, endothélium , monocytes/macrophages, récepteur des oestrogènes

Formation à la recherche

Coresponsable du Master 2 Recherche Physiopathologie - Ecole Doctorale Toulouse III
Accueil du Master 2 Recherche Sciences Chirurgicales - Paris

Coopérations / Partenariats

ANR 2005 et 2006 et 2009
EVGN (6è PCRD)
Laboratoires Pierre Fabre

Principales publications du laboratoire

- Gourdy P, Araujo LM, Zhu R, Garmy-Susini B, Diem S, Laurell H, Leite-de-Moraes M, Dy M, Arnal JF, Bayard F, Herbelin A. Relevance of sexual dimorphism to regulatory T cells: estradiol promotes IFN-gamma production by invariant natural killer T cells. Blood.2005 105(6): 2415-20.
- Arnal JF, Scarabin PY, Trémollières F, Laurell H and Gourdy P. Estrogens in vascular biology and disease: where do we stand today? 2007 Lippincott Williams & Wilkin
- Billon-Gales A, Fontaine C, Filipe C, Douin-Echinard V, Fouque MJ, Flouriot G, Gourdy P, Lenfant F, Laurell H, Krust A, Chambon P, Arnal JF. The transactivating function 1 of estrogen receptor {alpha} is dispensable for the vasculoprotective actions of 17{beta}-estradiol.
Proc Natl Acad Sci U S A. 2009;106:2053–2058
- Riant E, Waget A, Cogo H, Arnal JF, Burcelin R, Gourdy P.
Estrogens protect against high-fat diet-induced insulin resistance and glucose intolerance in mice. Endocrinology 2009, 150(5):2109-17.
- Toutain CE, Brouchet L, Raymond-Letron I, Vicendo P, Bergès H, Favre J, Fouque MJ, Krust A, Schmitt AM, Chambon P, Gourdy P, Arnal JF, Lenfant F.
Prevention of skin flap necrosis by estradiol [illegible] a protected vascular network. Circ Res. 2009; Jan 30;104(2):245-54.

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Atherothrombosis: role of oestrogens and novel therapeutic approaches

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An Inserm Team working in the Unit 1048, in association with Université de Toulouse III (I2MC, the Institute of cardiovascular and metabolic diseases).

Scientific objective

In the last years, our group contributed to evidence that, beside the prevention of osteoporosis, targeting estrogen signalling represents an attractive and effective perspective to prevent the development or the progression of atherosclerosis as well as type 2 diabetes.
We demonstrated that ERalpha, but not ERbeta is absolutely necessary for the vasculoprotective effects of E2 in atheroma, NO production and reendothelialization, as well as on insulin sensitivity and glucose tolerance.
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Expected health effects

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Key words

Atherome, endothelium, monocytes/macrophages, receiver of the oestrogens

Research training

Head of Master 2 Research Pathoyhysiologie - Ecole Doctorale Toulouse III
Accueil du Master 2 Research Surgical Sciences - Paris

Cooperation and Partnerships

ANR 2005 et 2006 et 2009
EVGN (6è PCRD)
Laboratoires Pierre Fabre

Principal laboratory publications

- Gourdy P, Araujo LM, Zhu R, Garmy-Susini B, Diem S, Laurell H, Leite-de-Moraes M, Dy M, Arnal JF, Bayard F, Herbelin A. Relevance of sexual dimorphism to regulatory T cells: estradiol promotes IFN-gamma production by invariant natural killer T cells. Blood.2005 105(6): 2415-20.
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