**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 targets, 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**

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.

**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**

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. 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.

Expected health effects
Our final goal is to open new perspectives regarding the modulation of ERα and β 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.

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

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

Principal laboratory publications
  Proc Natl Acad Sci U S A. 2009;106:2053–2058