**INTRODUCTION**

The steroid hormone 20-Hydroxyecdysone (20E) plays a key role in insect development through nuclear ecdysone receptors (EcRs) and at least one membrane receptor (DopEcR). Although mammals lack EcR, 20E displays pharmacological effects on mammals: for example, it stimulates protein synthesis and is marketed as a physical performance enhancer. Based on 20E physiological effects on muscle mass, a 20E based-drug termed BIO101 has been designed for the treatment/prevention of muscle pathologies, e.g. sarcopenia. However, the mechanism of action on mammals has not been elucidated. Thus, the goal of this study was to identify a receptor involved in 20E effects.

**EVIDENCE FOR INVOLVEMENT OF A MEMBRANE RECEPTOR**

We previously documented a dose-dependent inhibition of myostatin gene expression after treatment with 20E. In order to determine if this effect was mediated by a membrane receptor, we compared the effects of three 20E-protein conjugates respectively involving positions 2, 6 and 22 of the molecule on myostatin gene expression.

• We observed that two of them retained an activity close to that of free 20E, whereas the third one was inactive.

• These results show that the presence of a bulky protein does not prevent 20E activity, provided that the A ring remains free.

**IN VolVEMENT OF MAS RECEPTOR IN MEDIATING 20E EFFECT**

There are plenty of GPC receptors, thus to reduce our field of investigation, we performed a wide literature survey focusing on control of muscle cells, insulin sensitivity and fat mass gain. A set of 9 receptors was thus selected, and the only receptor which gave positive data was Mas, the receptor of angiotensin-(1-7).

• Mas receptor down regulation by Si RNA led to significant decrease of MAS receptor gene expression in all transfected group by directed SiRNA versus scramble SiRNA.

• IGF-1, 20E or Ang 1-7 inhibited significantly myostatin gene expression in cells transfected with scramble SiRNA.

• Down-regulation of Mas receptor gene did not allow inhibition of myostatin gene after treatment with 20E or Ang 1-7.

**CONCLUSION**

20E was shown to enlarge fiber size in vitro and increase protein amounts in vivo. These effects are associated with the inhibition of myostatin gene expression. Cellular signaling studies showed that 20E involves the activation of MAS receptor. These results led us to design a clinical trial on obese sarcopenic patients with BIO101.