

Identification de gènes candidats “muscle lisse” pour le syndrome POIC

Appel à projet FIMATHO 2021



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Development of
visceral smooth muscle

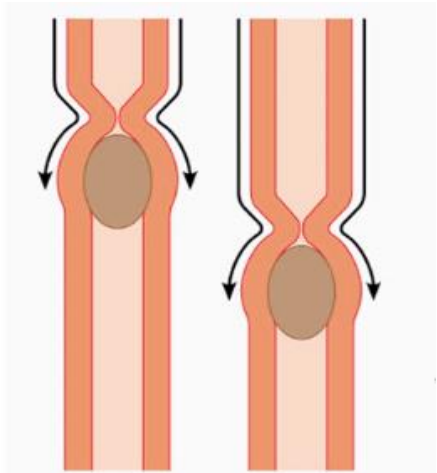


 **Inserm**

De l'organe à l'appareil contractile

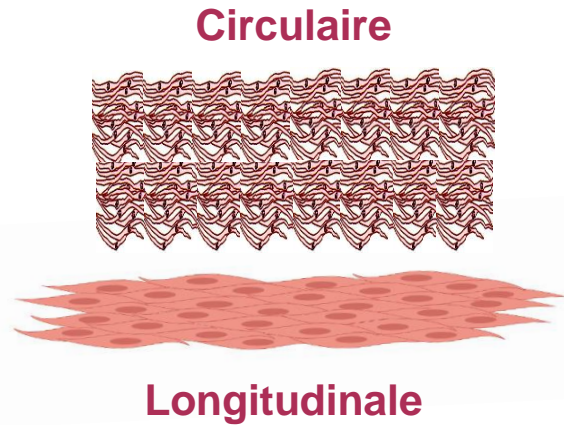


Motilité digestive

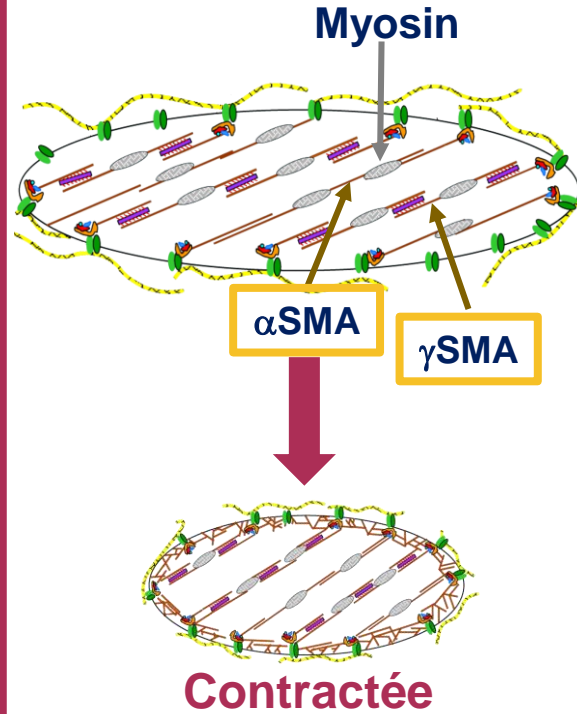


Bol alimentaire

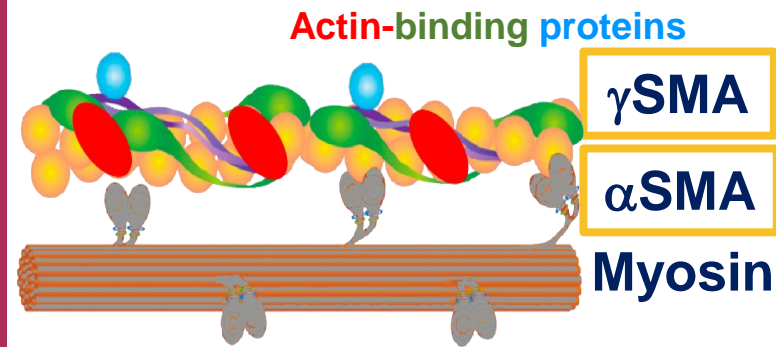
Muscles lisses digestifs



Cellule musculaire lisse relaxée



L'appareil contractile



Syndrome POIC: génétique et muscle lisse



Segregation of a Missense Variant in *Enteric Smooth Muscle Actin* γ -2 With Autosomal Dominant Familial Visceral Myopathy

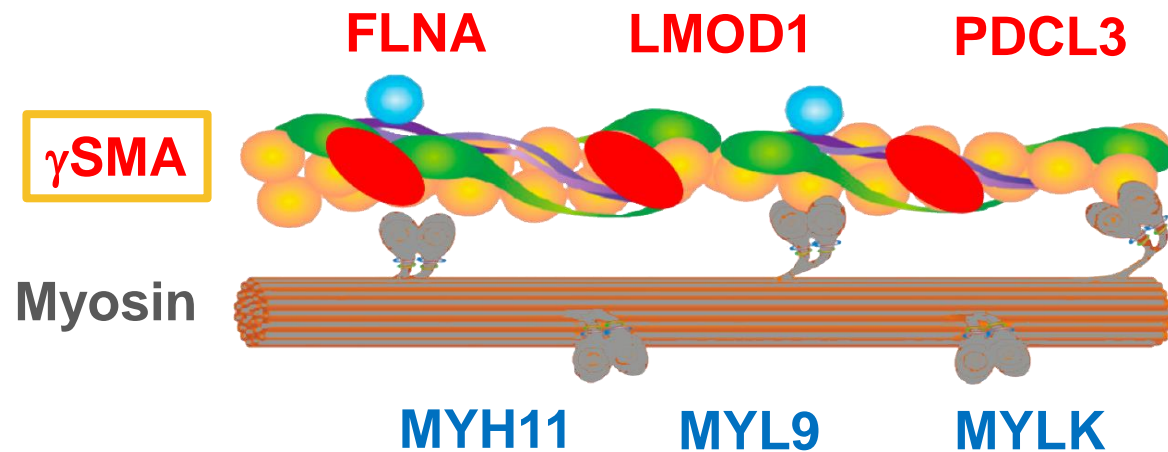
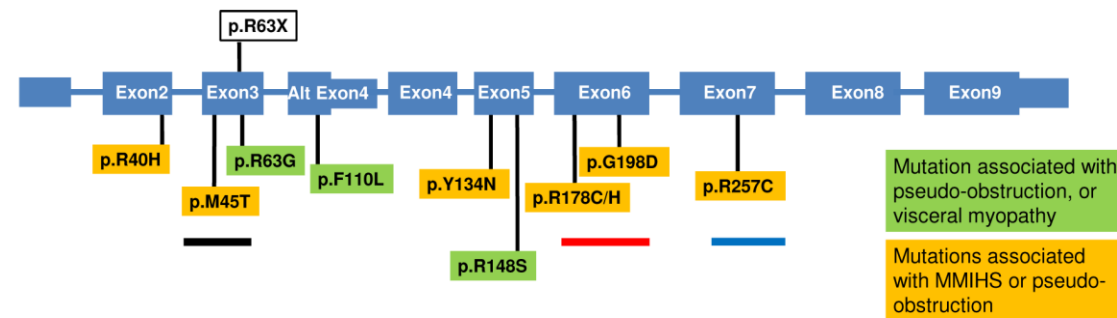
HELI J. LEHTONEN,* TAINA SIPPONEN,† SARI TOJKANDER,§ RIITTA KARIKOSKI,|| HEIKKI JÄRVINEN,¶ NIGEL G. LAING,# PEKKA LAPPALAINEN,§ LAURI A. AALTONEN,* and SARI TUUPANEN*

GASTROENTEROLOGY 2012;143:1482-1491

Le gène *ACTG2* code pour la protéine γ SMA !!!

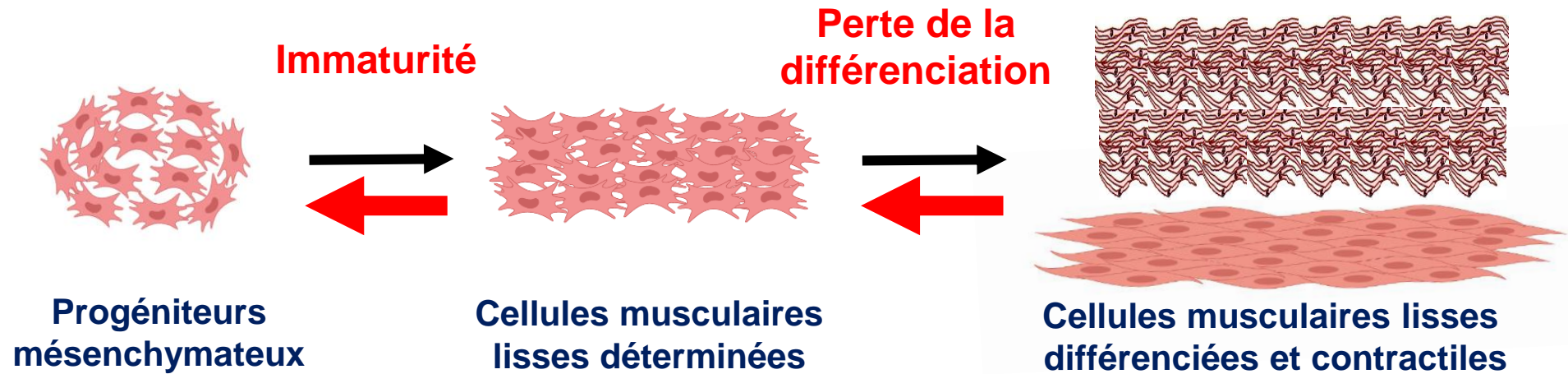
Les variants *ACTG2* sont rencontrés chez les patients POIC pédiatriques dans 40%-45% (Rendu J.).

Des variants perte de fonction sont retrouvés moins fréquemment dans les gènes *Filamin A (FLNA)*, *Leimodin 1 (LMOD1)*, *Phosducin Like 3 (PDCL3)*, *Myosin heavy chain 11 (MYH11)*, *Myosin Light Chain 9 (MYL9)* et *Myosin light chain kinase (MYLK)*.



**Appareil contractile des cellules musculaires lisses :
cible principale du syndrome POIC !!!**

Développement et Dédifférenciation du muscle lisse digestif



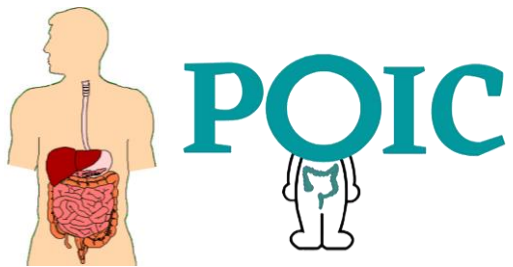
LIX1

γ SMA : gamma Smooth Muscle Actin

α SMA : alpha Smooth Muscle Actin

Actin-binding proteins (FLNA, LMOD1...)

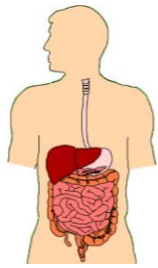
Myosin proteins (MYLK, MYL9...)



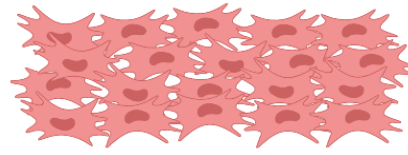
Identification des mécanismes altérés chez les patients POIC

Notarnicola et al, *Gastroenterology*, 2012
McKey et al, *BMC Biol*, 2016
Guérin et al, *Redox Biol*, 2022

Les travaux de l'équipe financés par FIMATHO

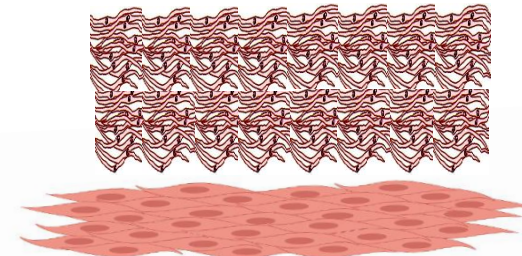
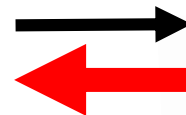


LIX1

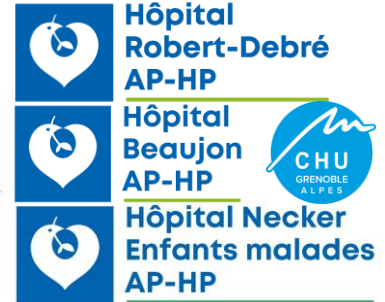


γ SMA

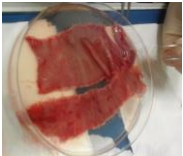
α SMA



Actin binding proteins



Intestin
POIC



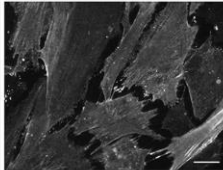
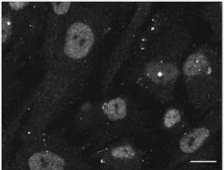
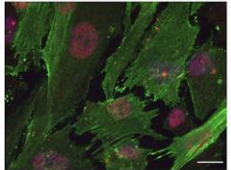
SMCs
POIC

α SMA/MYOCD/Nuclei

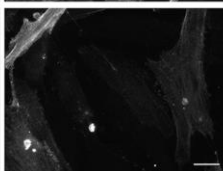
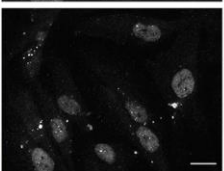
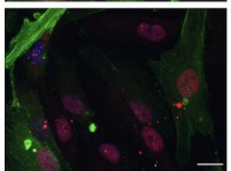
MYOCD

α SMA

CTL1



CIP01



**Les SMCs des patients POIC
présentent une altération de leur
différenciation**

Martire et al., *J Cell Mol Med* 2021

DONNEES NON PUBLIEES

~~Données non publiées~~ Données non publiées

Equipe “Développement du muscle lisse viscéral & pathologies associées”



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Development of visceral smooth muscle

