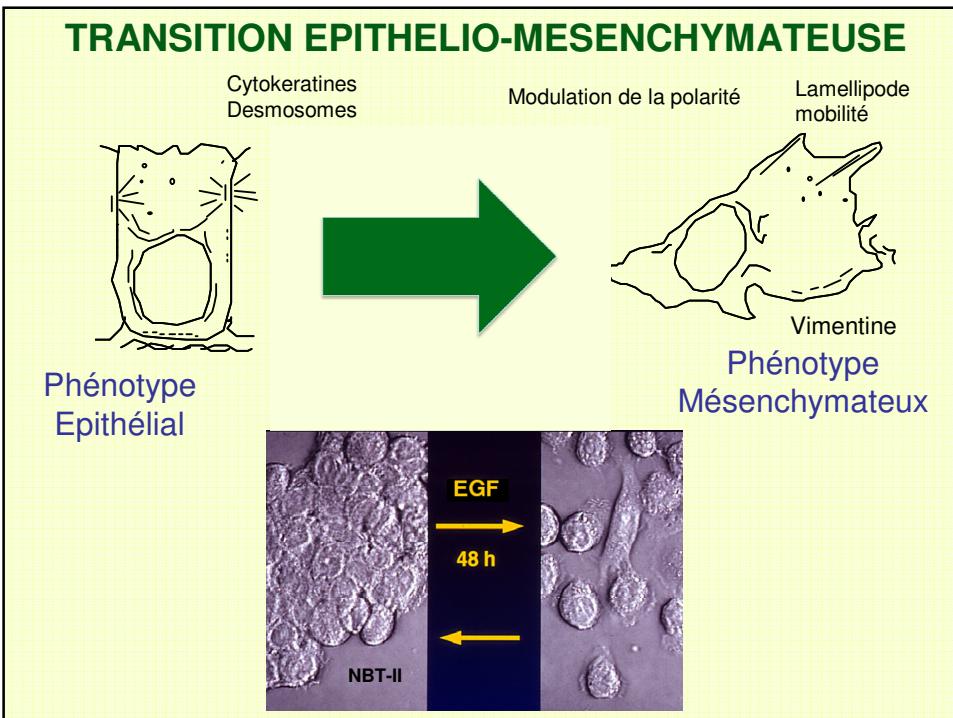


Transition épithélio-mésenchymateuse et réparation des blessures cutanées

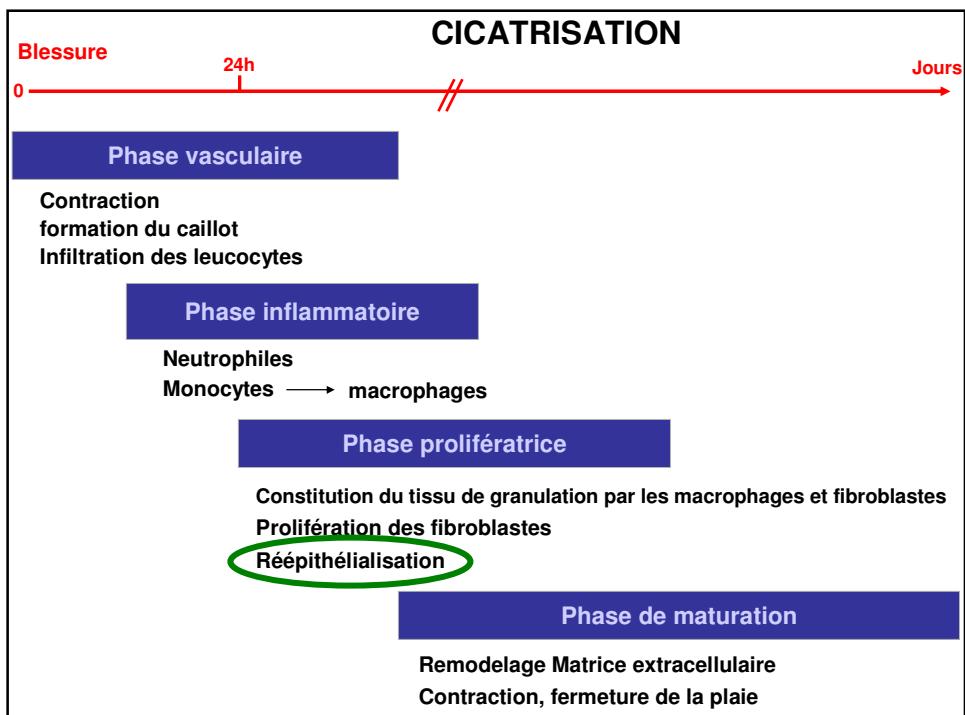
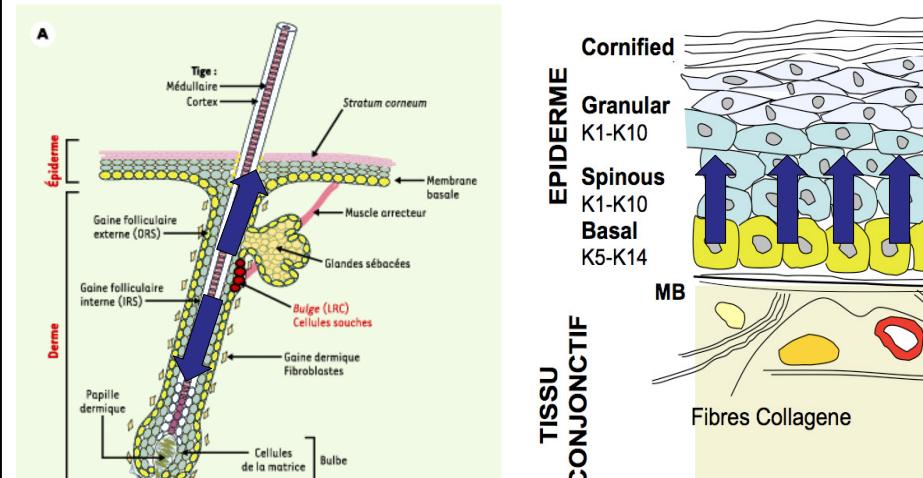
Séance commune Académie nationale de médecine, Académie nationale des sciences: La Plasticité cellulaire: de l'embryon à la fibrose et au cancer

Mardi 1^{er} décembre 2009

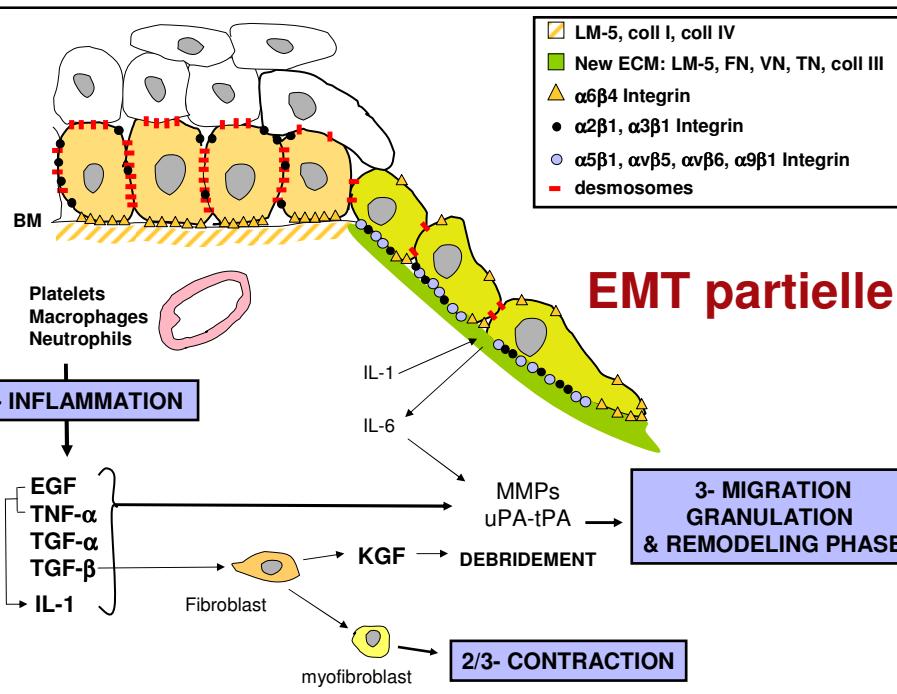
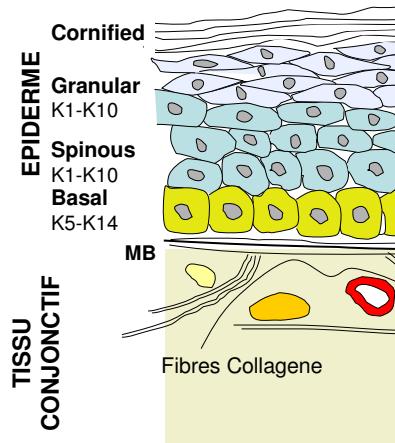
Pierre Savagner



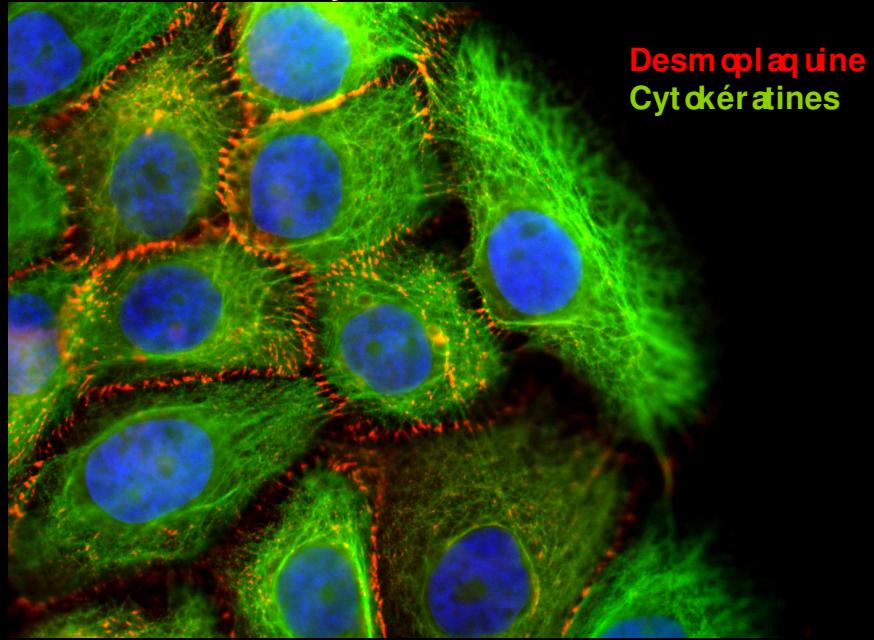
LES MIGRATIONS SONT PARTIES INTEGRANTES DE LA VIE D'UN KERATINOCYTE



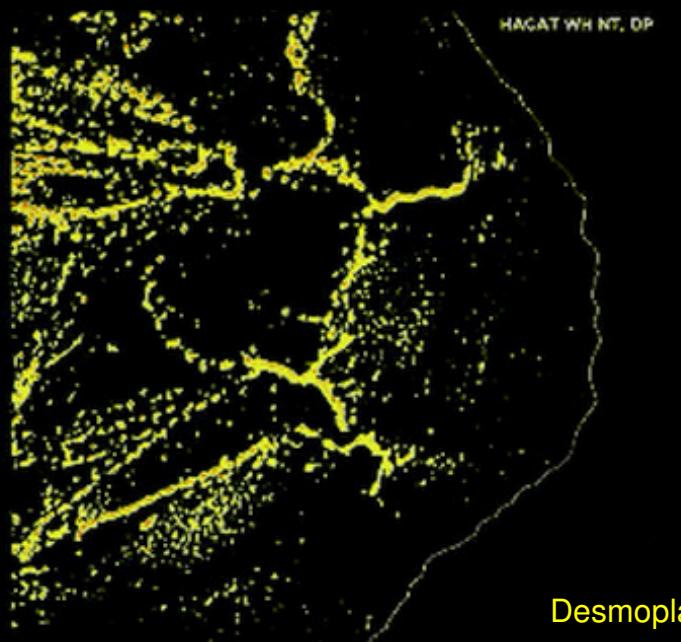
Blessure dans l'épiderme



**L'acétrification implique une dissociation partielle
des kératinocytes du front invasif**



Des espaces vides apparaissent entre les desmosomes



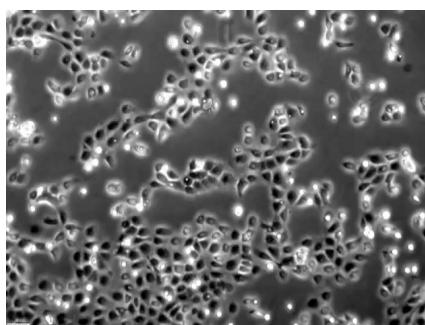
EMT partielle: Les cellules maintiennent des structures adhésives au cours de la migration



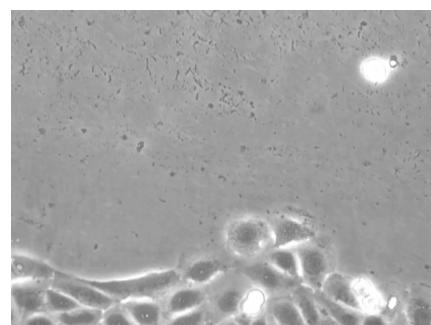
KERATINOCYTES (RAC Δ-GFP)

Le mode de migration et l'intensité de l'EMT sont contrôlés par des équilibres dynamiques entre les structures d'adhésion cellule-cellule et cellule-sousstrat

**Sous confluence: EMT partielle à totale, cellules isolées en migration
Confluence (blessure): EMT partielle, cellules migrant en cohorte**

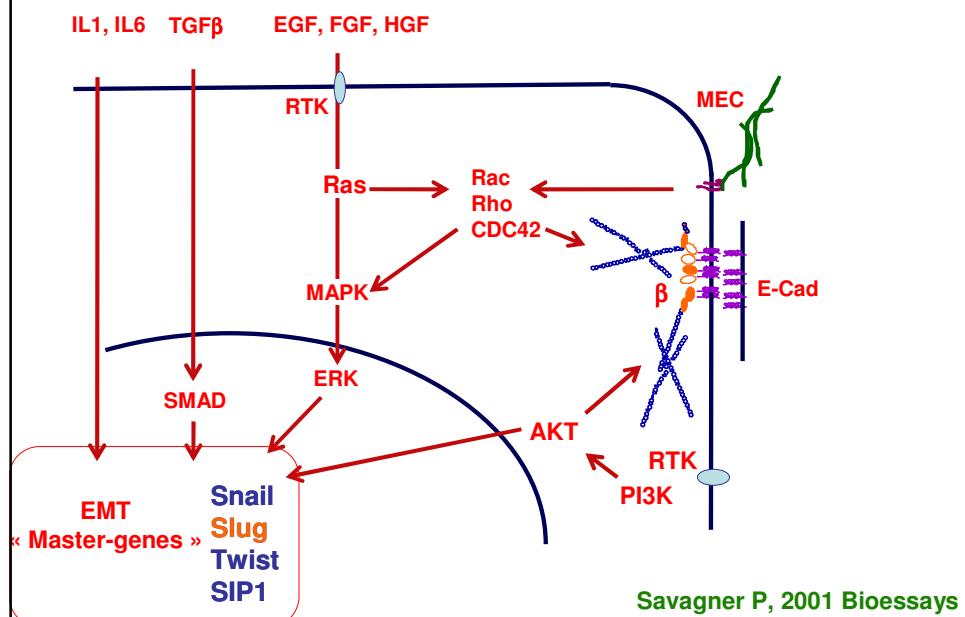


Kératinocytes sous-confluents

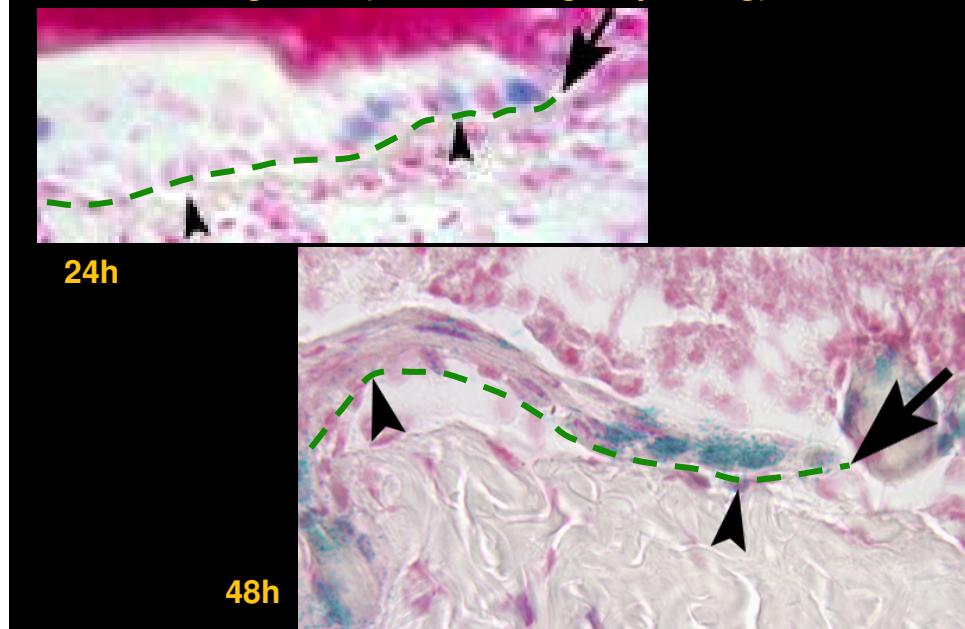


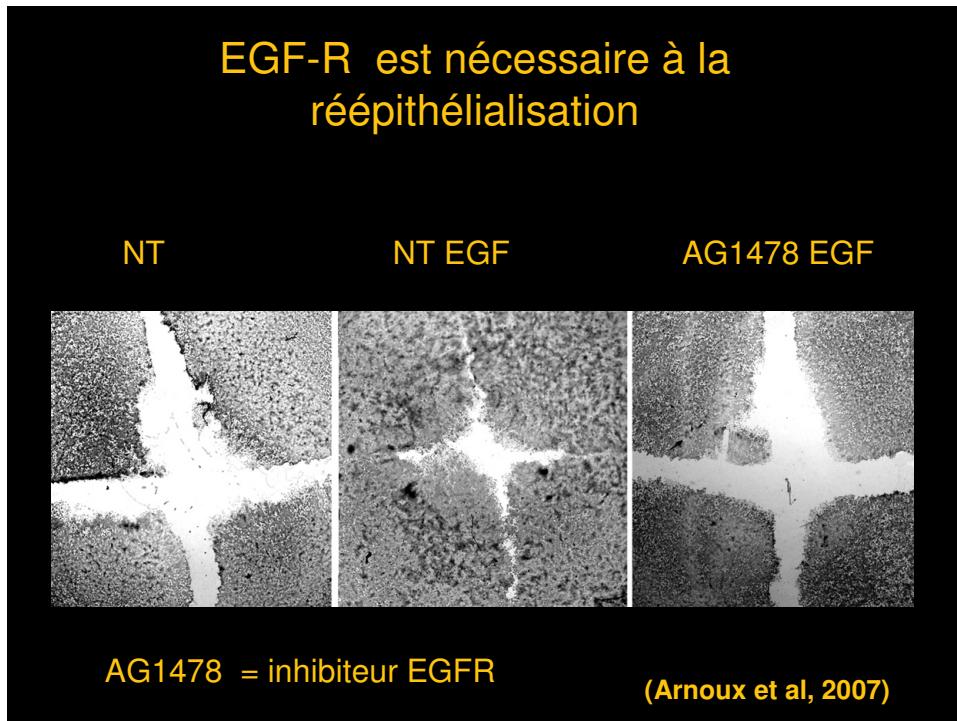
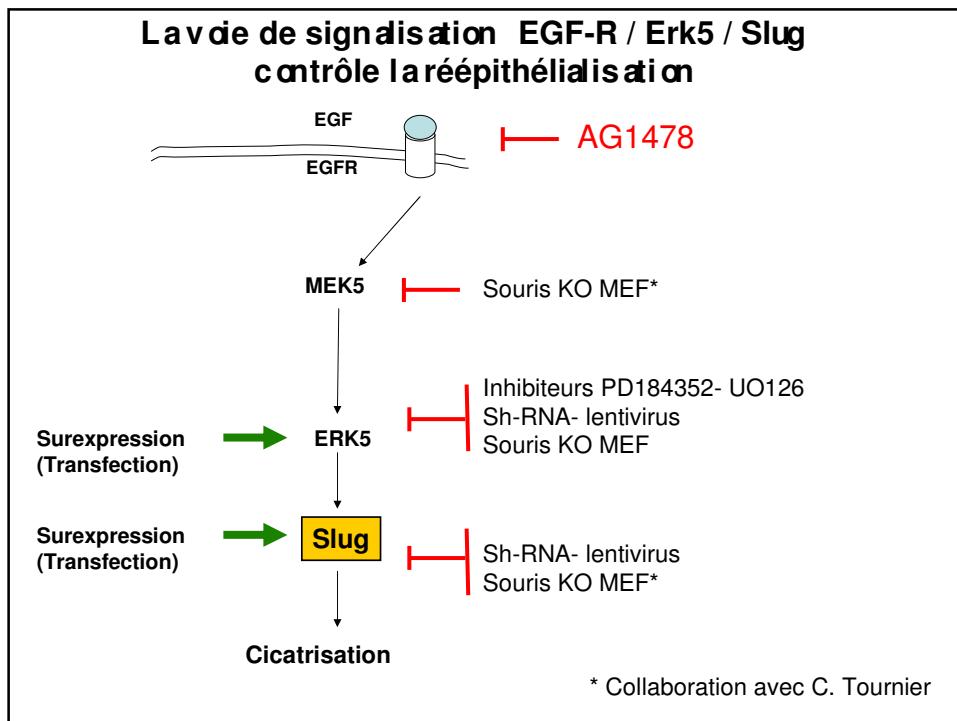
Kératinocytes confluents
(cicatrisation)

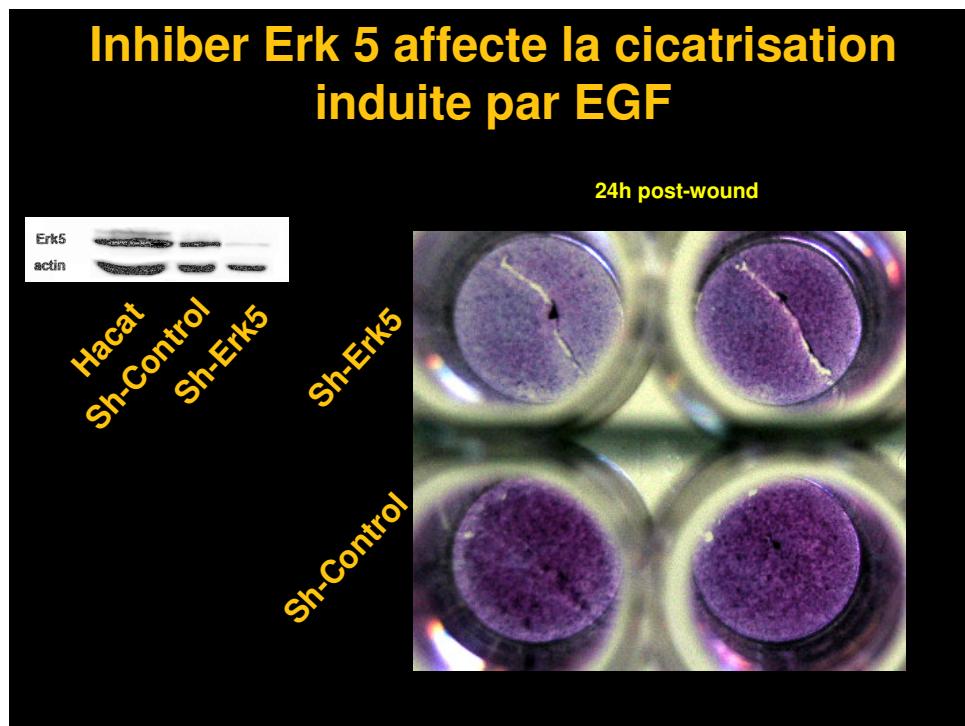
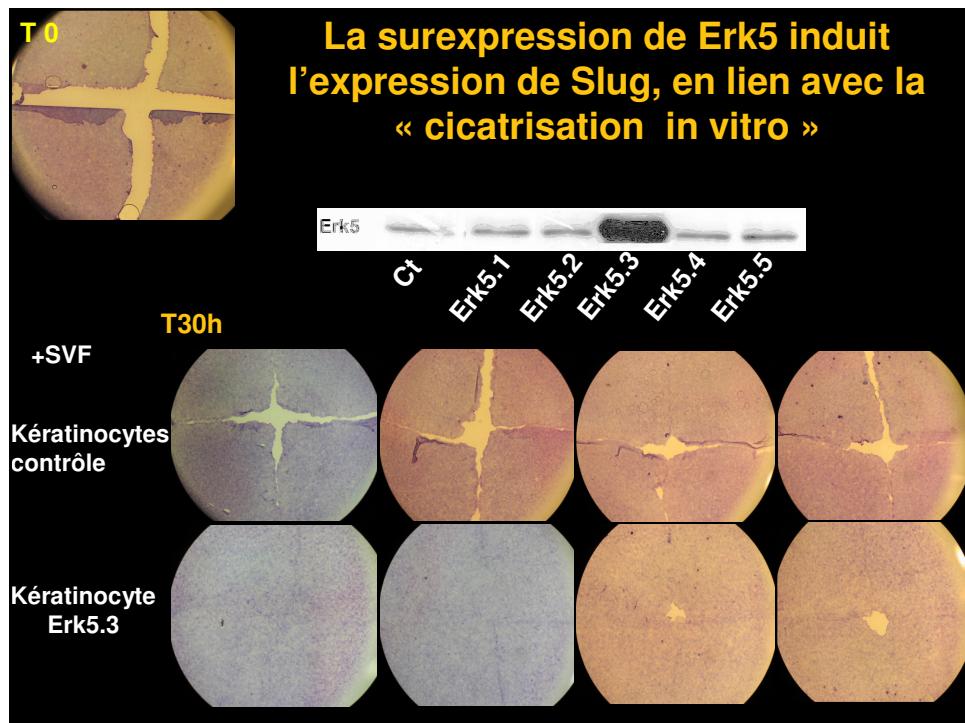
Les facteurs de cicatrisation contrôlent des voies de signalisation EMT



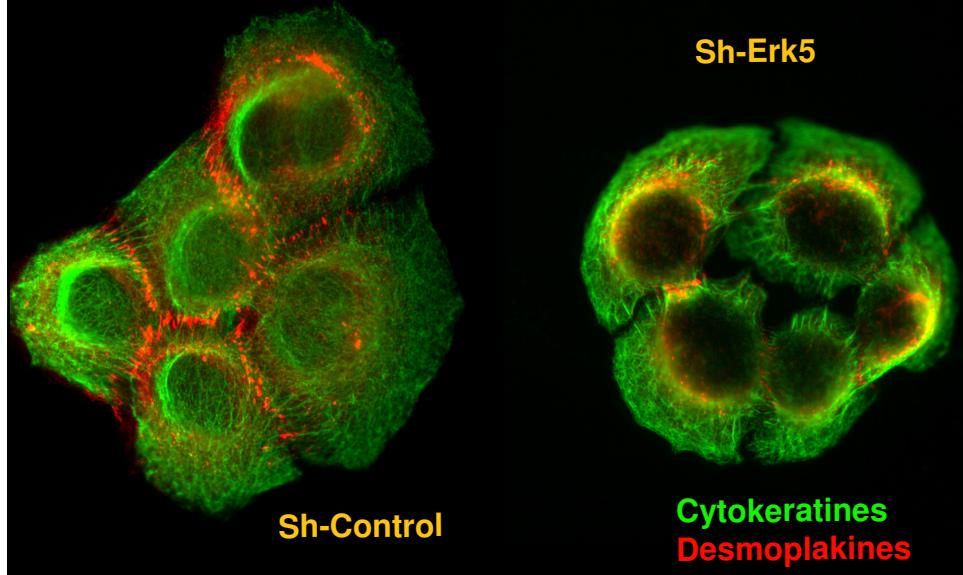
Expression de Slug dans les kératinocytes du front de migration (Souris transgénique Slug)



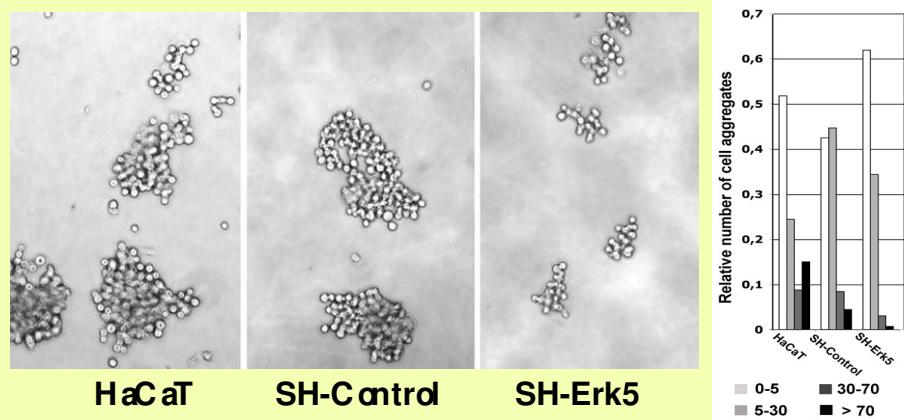




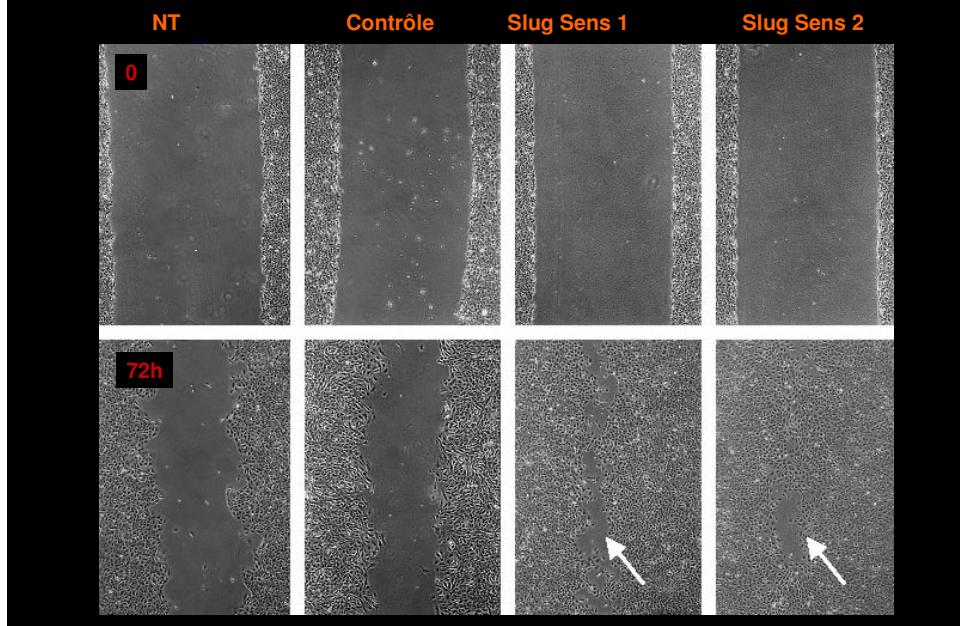
L'organisation des desmosomes de Kératinocyte Sh-Erk5 cells est perturbée



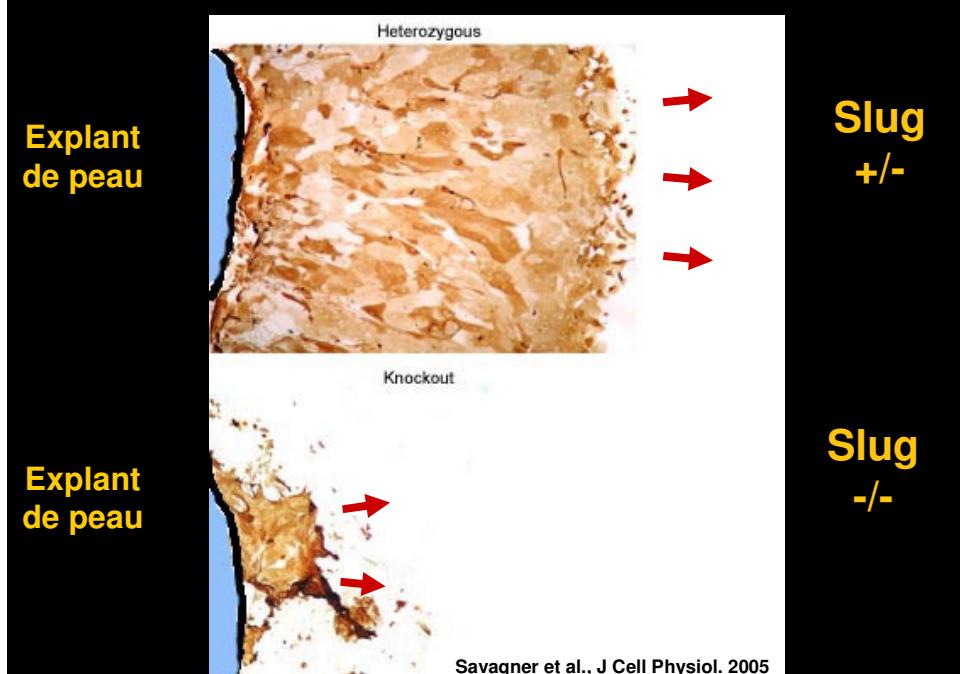
Erk5 contrôle l' aggrégation inter-cellulaire



LA SUREXPRESSION DE SLUG ACCELERE LA « CICATRISATION IN VITRO »

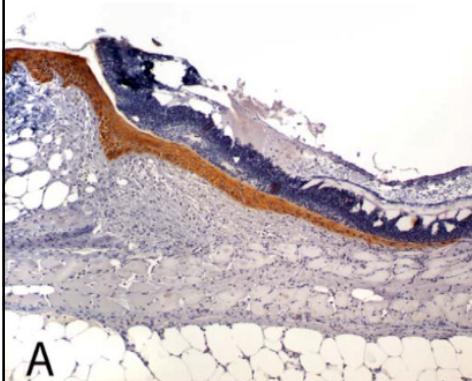


SLUG EST NECESSAIRE POUR UNE REEPITHELIALISATION EX-VIVO



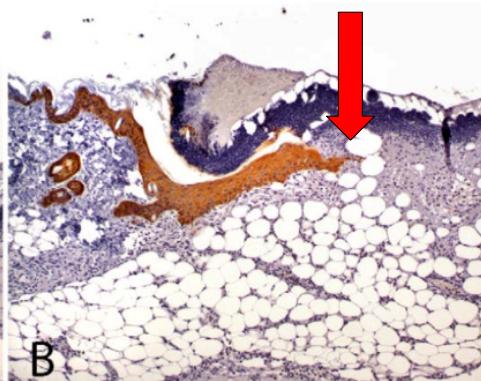
**L'absence de Slug compromet la réépithélialisation
In vivo dans la souris**

Contrôle



A

Slug KO



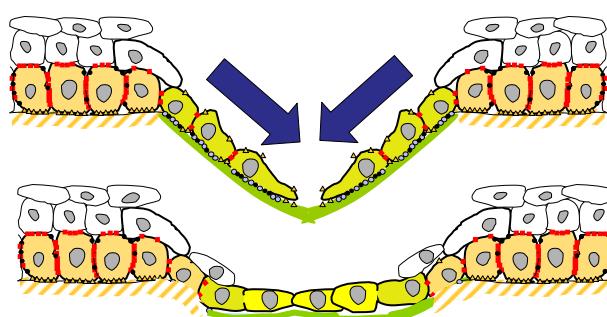
B

CYTOKERATINE 14

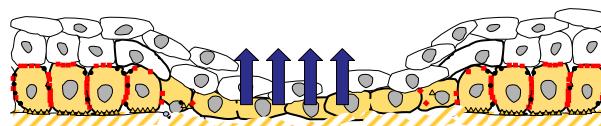
Hudson et al, J Dermatol Sci. 2009, 56:19-26.

Réépithélialisation: TEM partielle et temporaire

TEM partielle: migration



TEM temporaire: différenciation (migration)



Support

Fondation de France, Ligue Nationale contre le Cancer, GEFLUC-LR
Association pour la Recherche sur le Cancer



Collaborations

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L. Larue	Institut Curie, Orsay, France

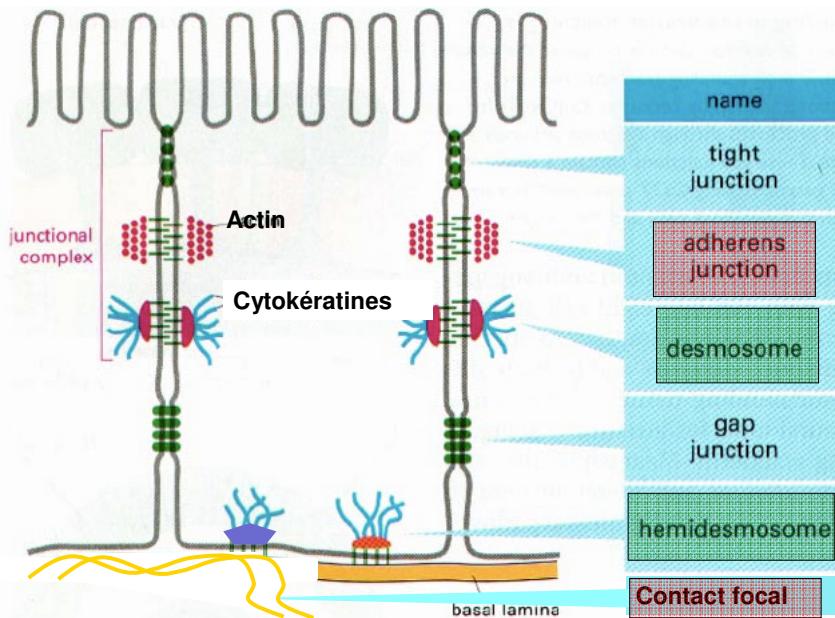
U868 INSERM, CRLC-Val d'Aurelle, Montpellier

TEM TEAM: Metastable Phenotypes

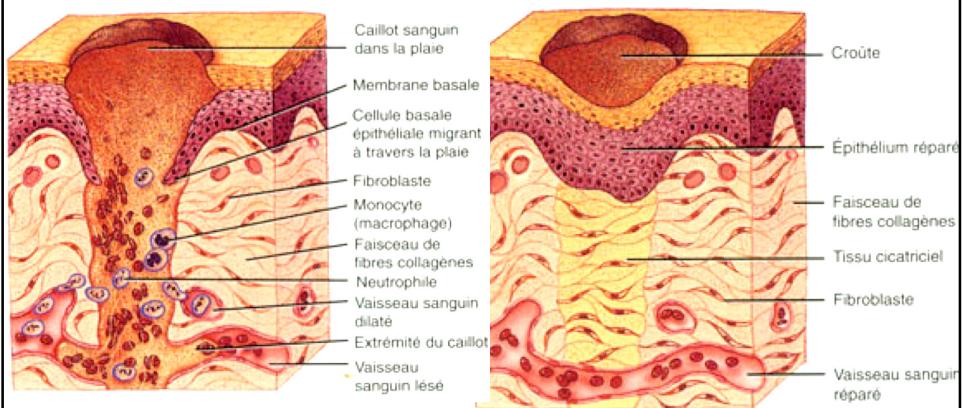
*V. ARNOUX1	PhD Student
*C. COME 2	PhD Student
*H. FONTAINE 3	Lab Tech
*F. MAGNINO 4	Post-Doc
M. NASSOUR	PhD student
P. SAVAGNER 5	CNRS, Team leader
H. VALLES 6	Lab Tech



Jonctions cellulaires épithéliales



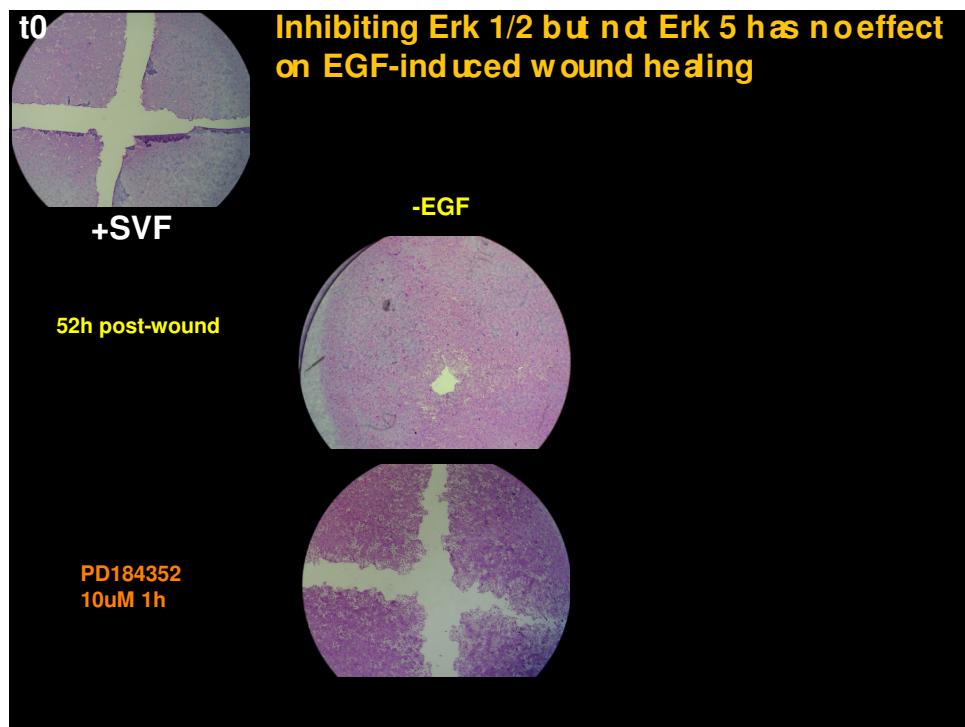
La cicatrisation cutanée fait intervenir une transition épithélio-mésenchymateuse partielle des kératinocytes « activés »



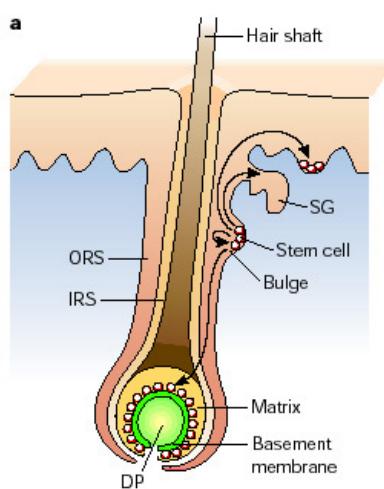
Activation des kératinocytes basaux (supra-basaux):

- remodellement cytosquelette (CK)
- migration cohésive

Tortora, Principes d'anatomie et de physiologie
Ed. De Boeck université)



Différentes niches pour différentes cellules souches



Cellules souches peau