

Journal Club Presentation 18.05.15

By Christoph Glogner

Gram negative bacteria increase non-small cell lung cancer metastasis via toll-like receptor 4 activation and mitogen-activated protein kinase phosphorylation

by Simon C. Chow et al.

Published in the International Journal of cancer

What did they want to know?

- Does TLR4 activation with heat-inactivated gram-negative bacteria cause an enhanced migration and adhesion of these cancer cells?
- If yes, which pathways are activated?
- Is there a way to block these pathways?

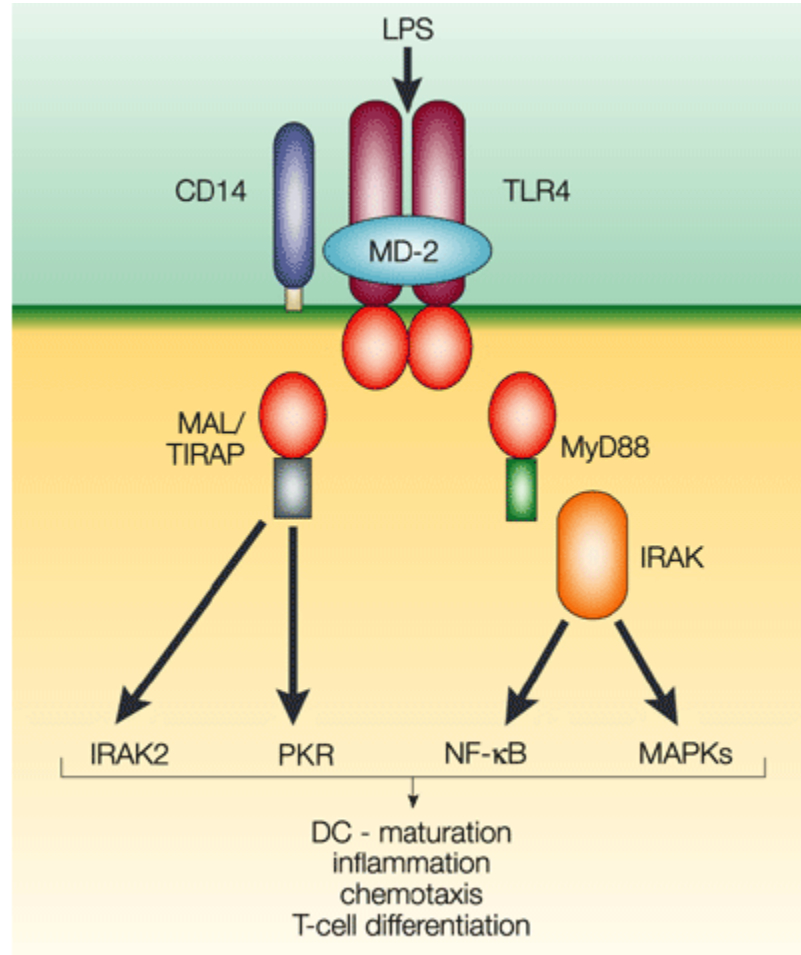
What is already Known?

- Pulmonary epithelium is barrier as well as part of the sentinel system
- enhanced migration and adhesion of cancer cell after activation of TLR4 due to LPS
- Postoperative infections decrease the 5-year overall and cancer-specific survival
- Most of these pulmonary infections are caused by gram- negative bacteria

What about TLR4?

- Activated by PAMPs for example LPS
- Part of a highly conserved receptor family
- Transmembrane Protein
- Dimerization if activated
- Signalpathway via MyD88 and MAPK as p38, ERK1/2 and JNK
- Leads to a defending reaction and synthesis of inflammatory cytokines

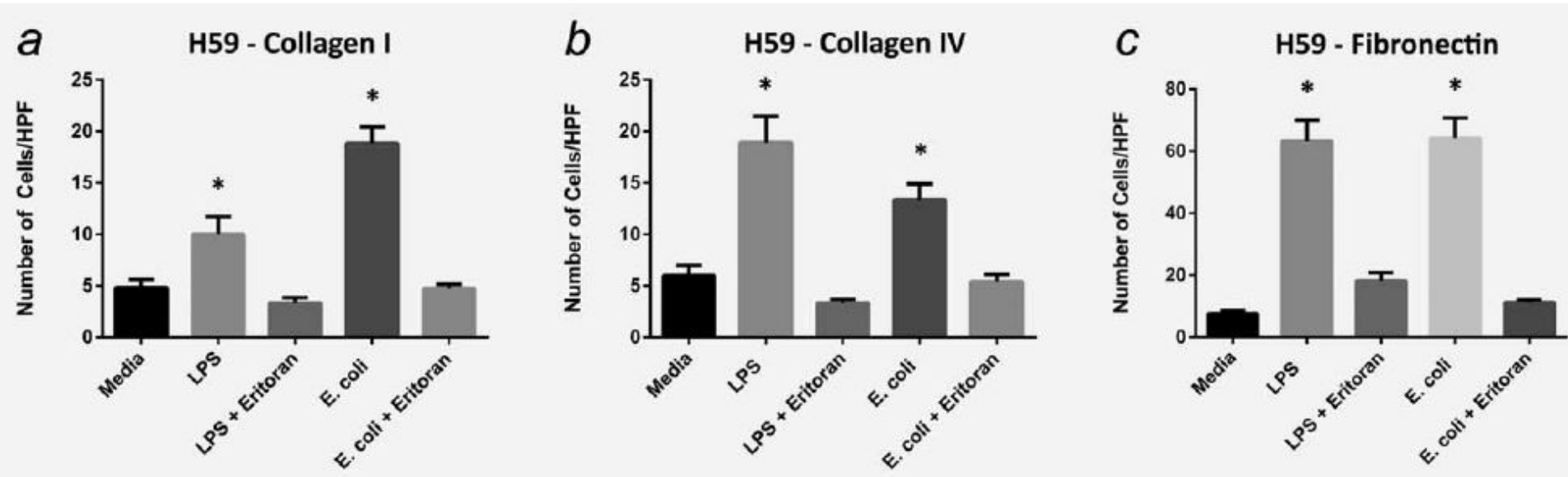
In a nutshell ...



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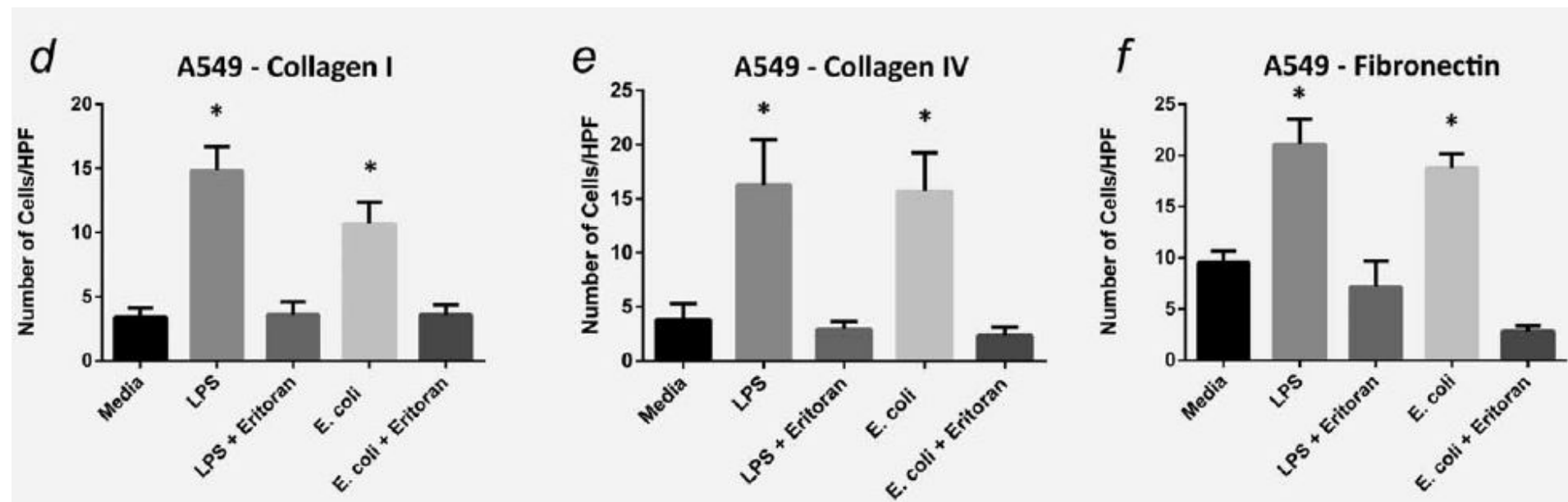
Results

Measurement of cell adhesion in H59 cells ...



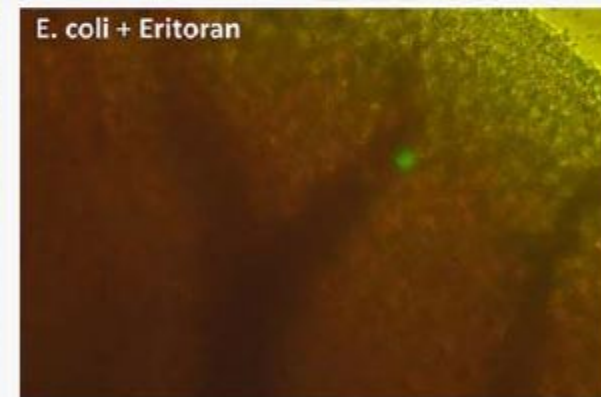
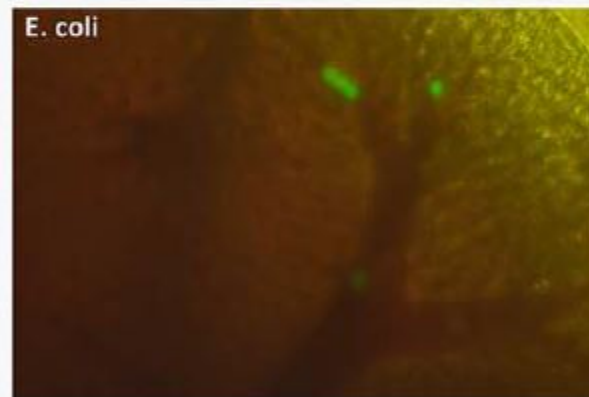
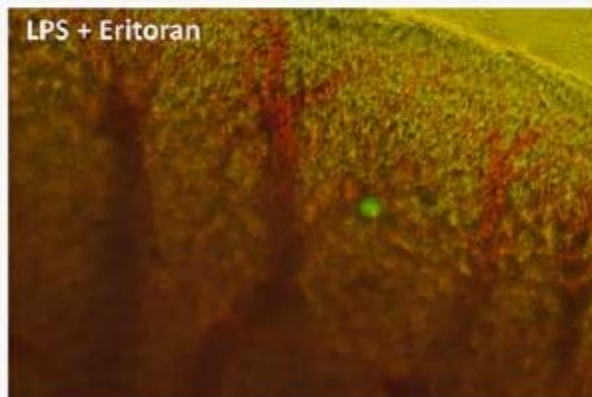
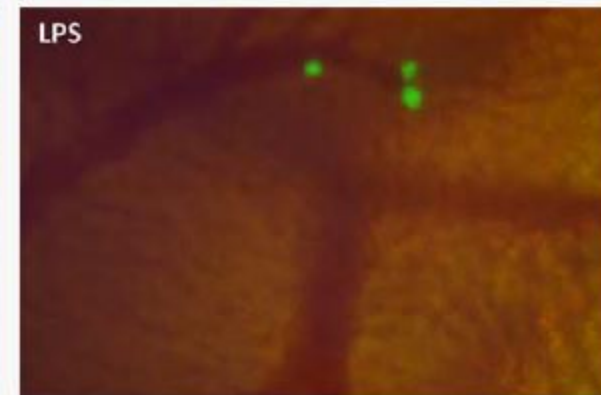
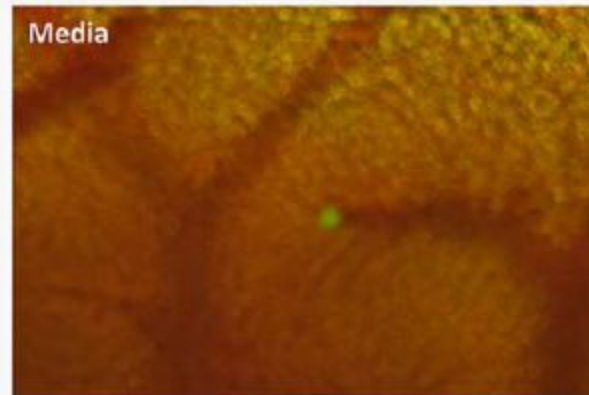
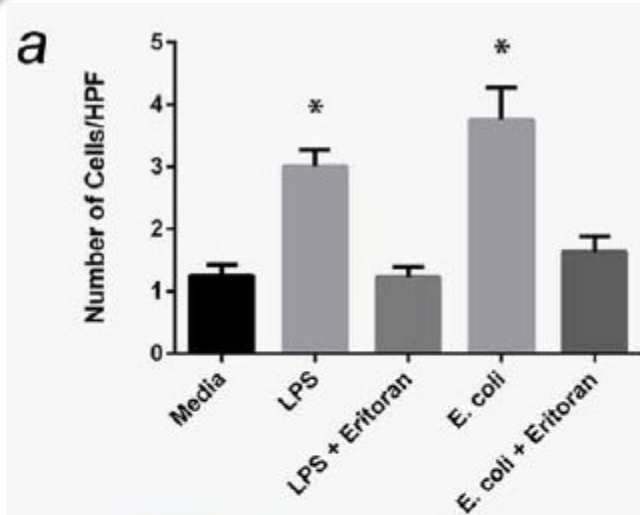
Count of adherent cells per High-Power-Field

... and A549 cells



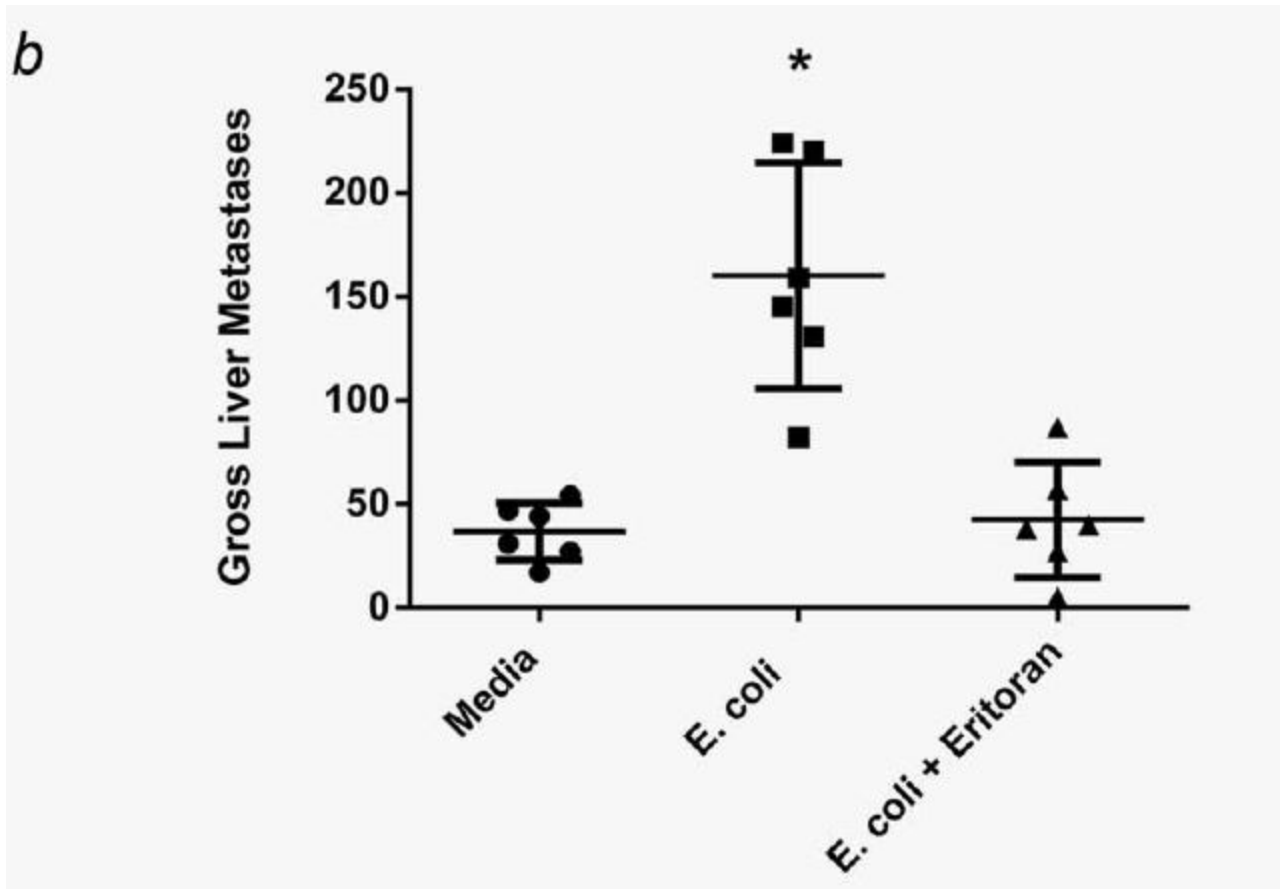
Count of adherent cells per High-Power-Field

In-Vivo measurement of Adhesion of cancer cells



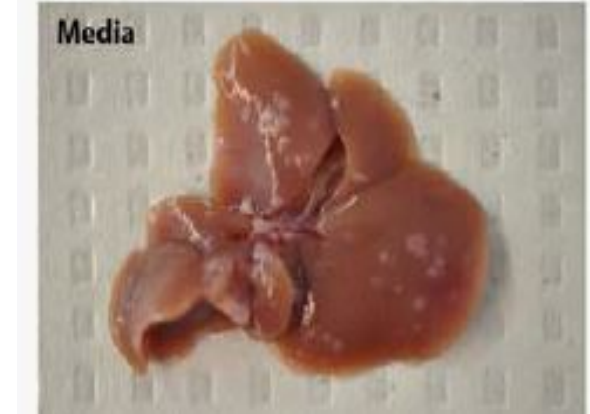
Count of adhesive cancer-cells in mouse-liversinusoids and some examples

In-Vivo Consequences



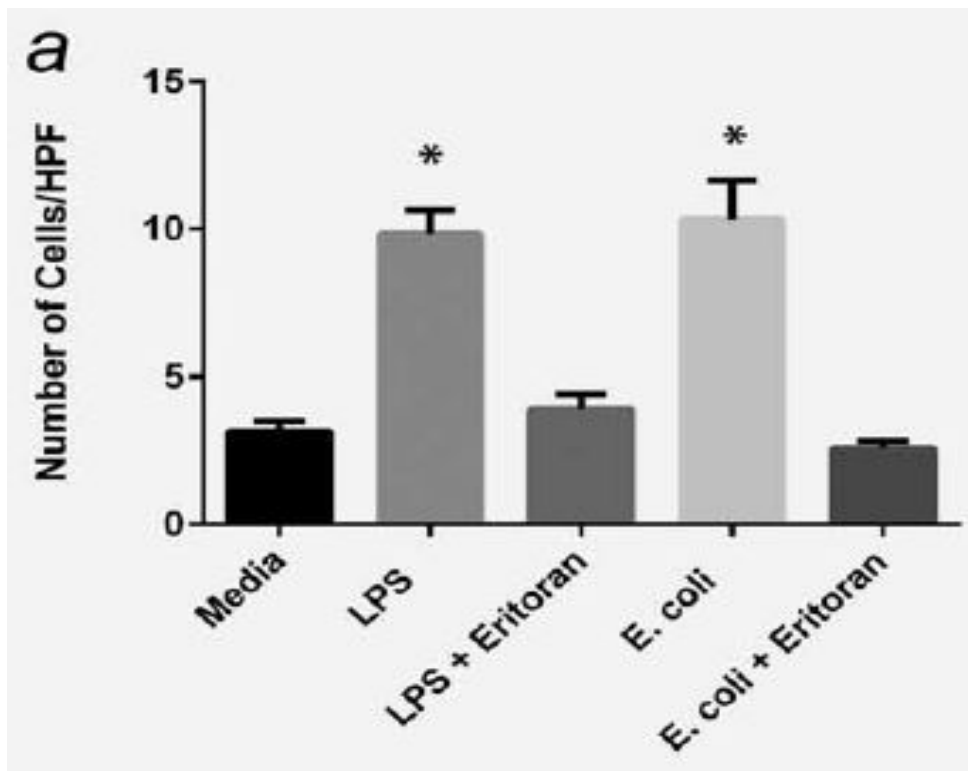
Count of metastases in harvested mouse livers 2 weeks after intrasplenic injection of H59 cells

In-Vivo Consequences in a macroscopic view



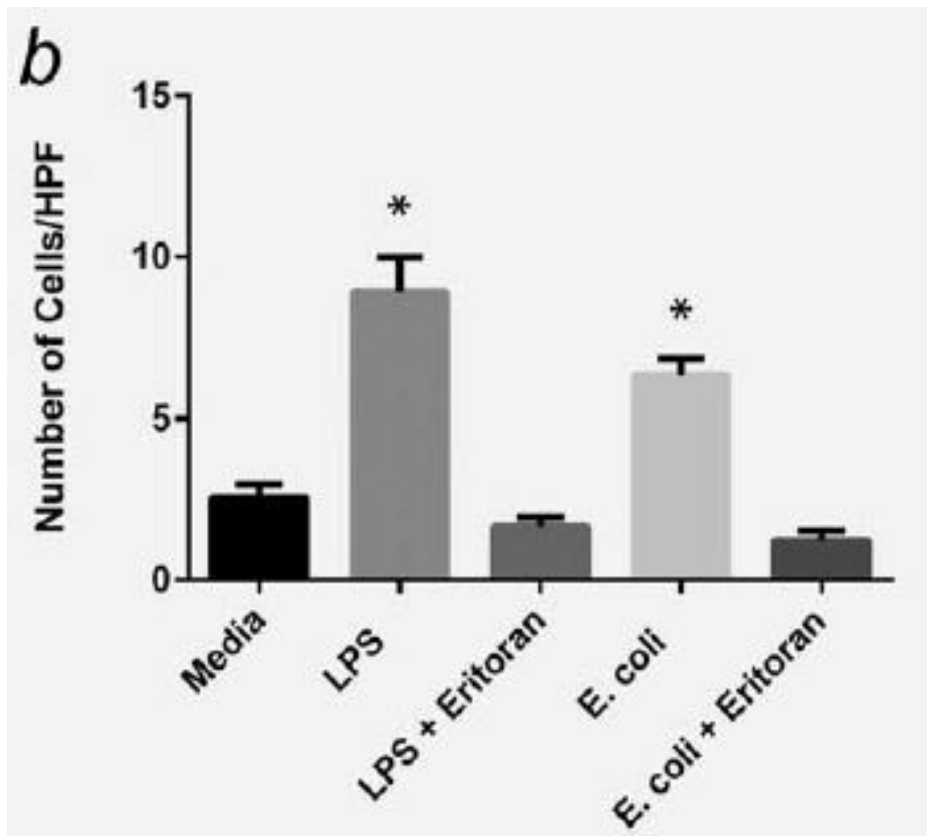
Examples of mouse-livers two weeks after the intrasplenic injection of H59 cells

Measurement of Migration of H59 cells ...



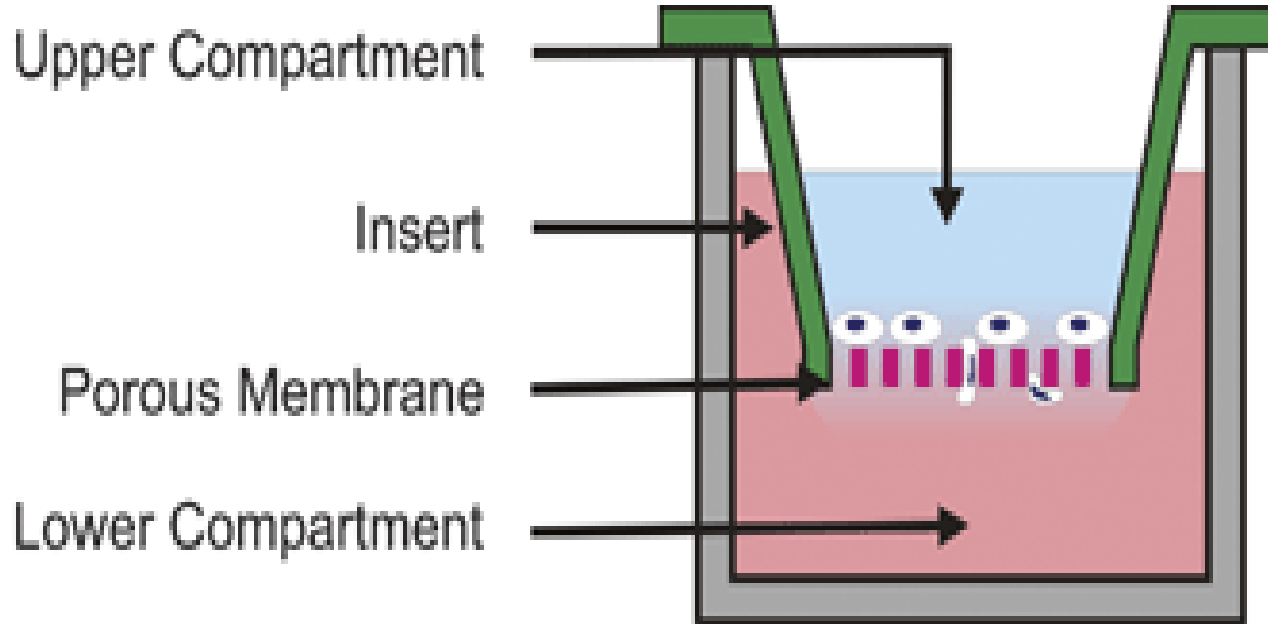
Count of cells per
High-Power-Field in
the lower chamber
after 24 h

...and in A549 cells



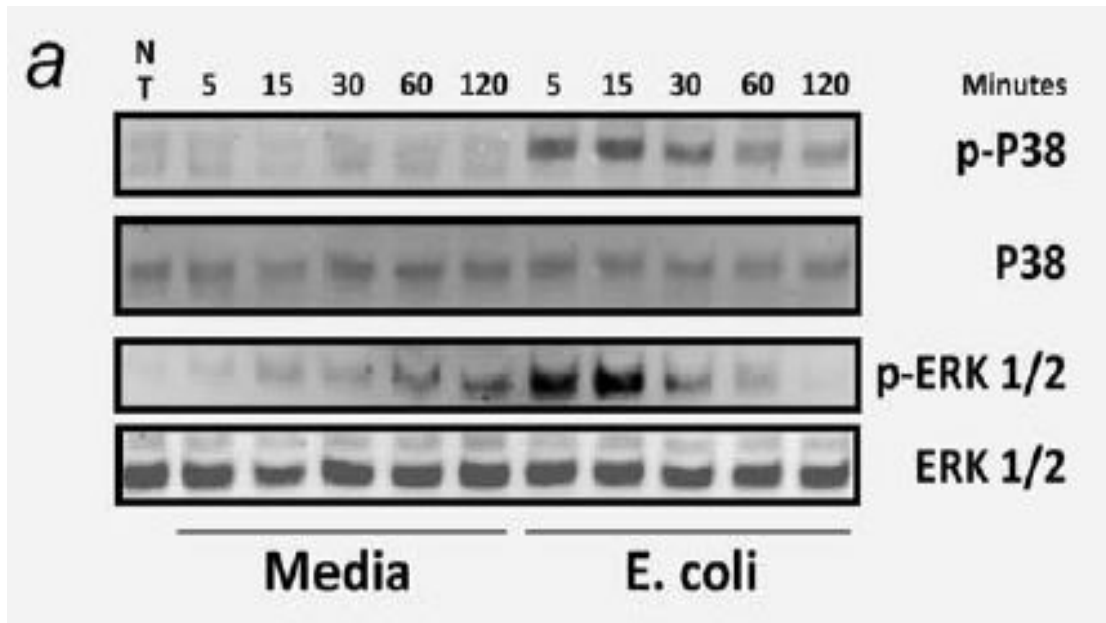
Count of cells per High-Power-Field in the lower chamber after 24 h

How this was done

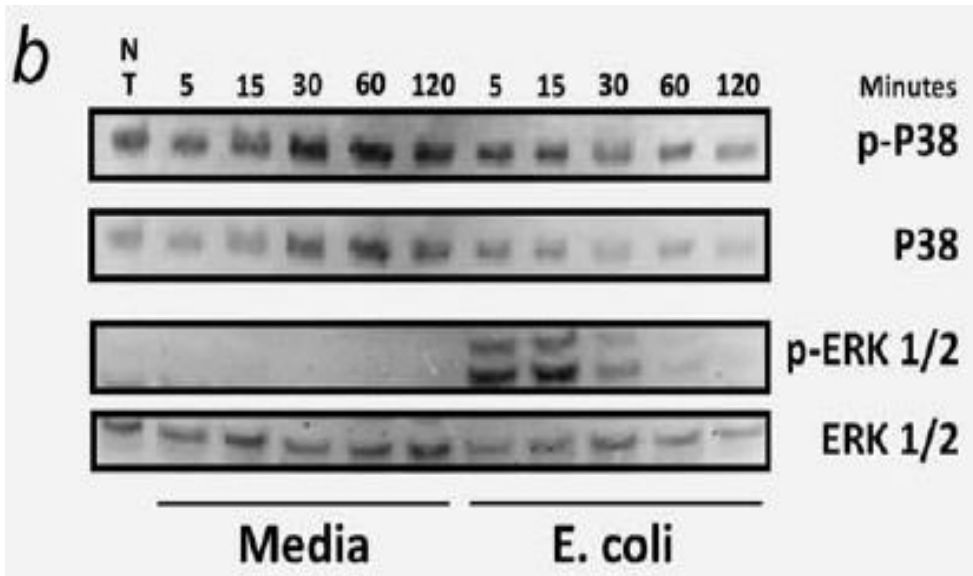


What happens inside the H59 cell

Western-Blot

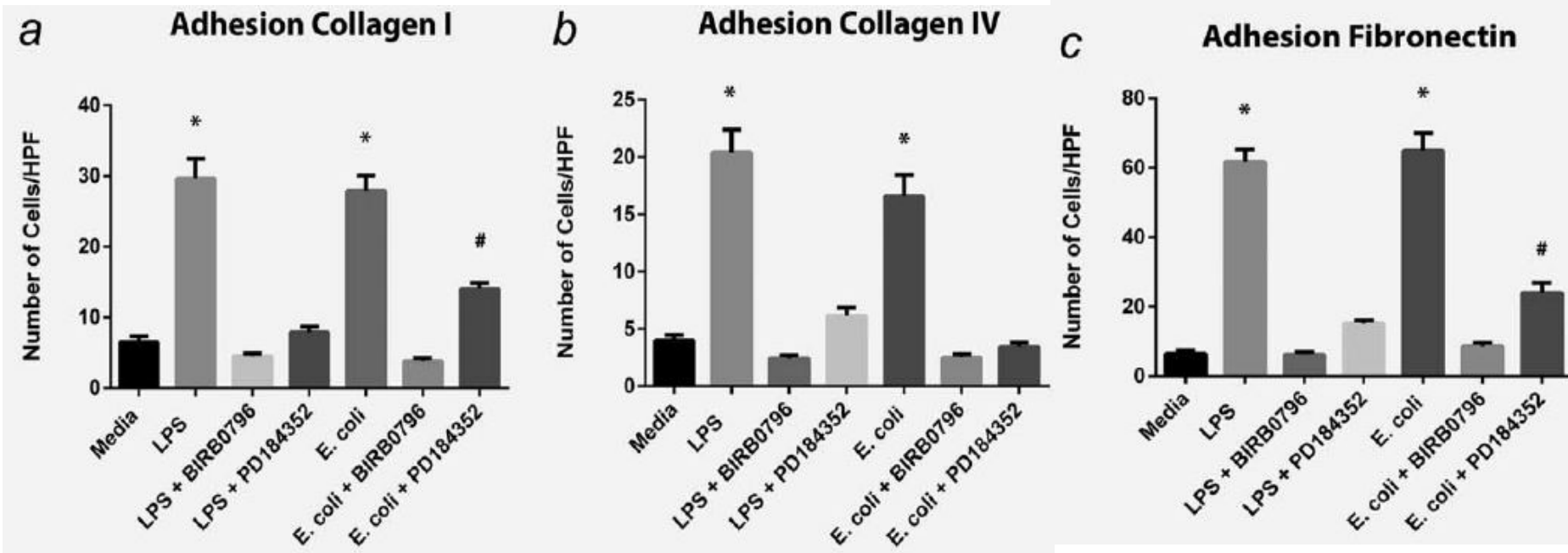


What happens inside the A549 cells



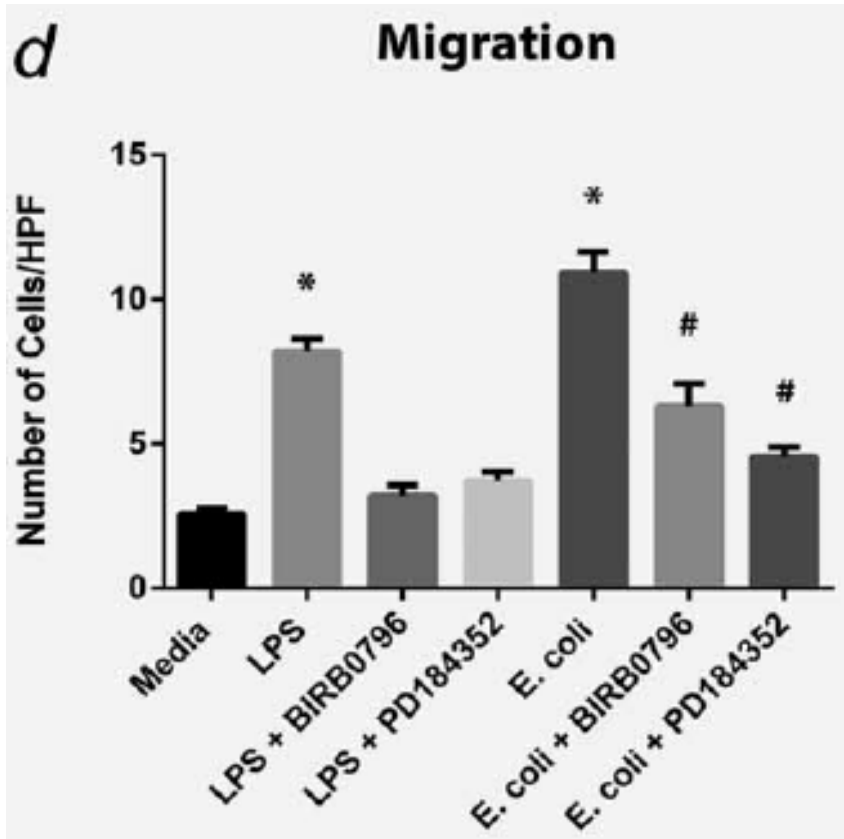
Westernblot

Blockade of the intracellular Cacade



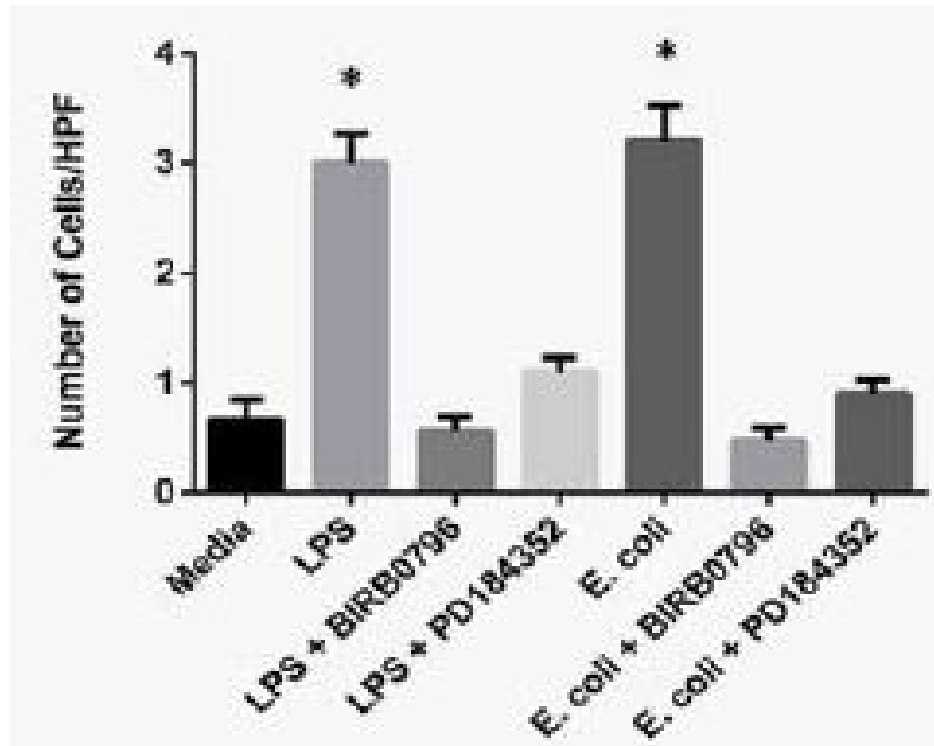
Counts of adhesive cell per High-Power-Field in Adhesion-Assays

You shall not pass



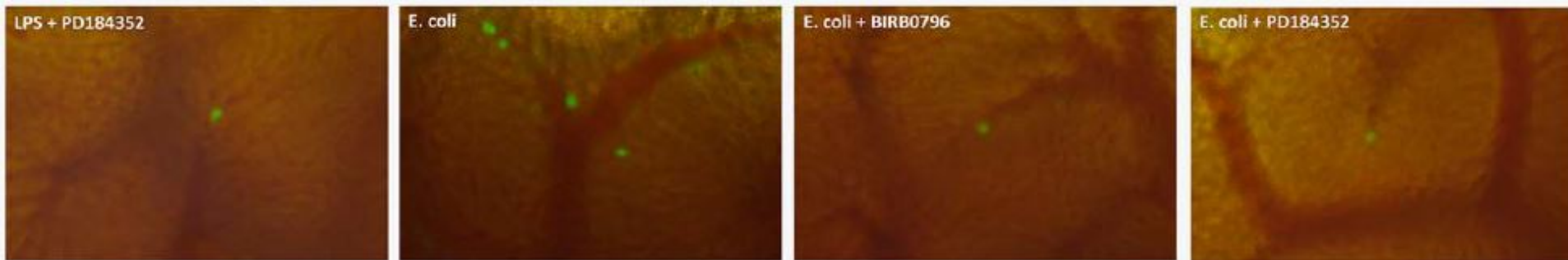
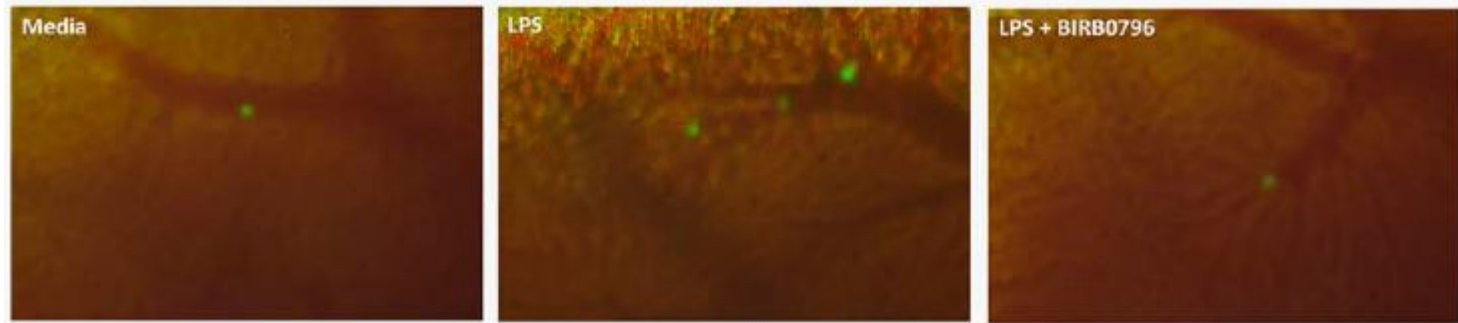
Cellcounts per High-Power-Field after Migrationassays

In-Vivo Blockade of the pathways



Cellcounts per High-Power-Field of mouse-livers after intrasplenic injection of H59 cells

Just because it's so beautiful



Examples of In-Vivo inverted fluorescence microscopy pictures of mouse-livers after intrasplenic injection of H59 cells



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Finally Done!



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Last one

References

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- <http://pubs.rsc.org/services/images/RSCpubs.ePlatform.Service.FreeContent.ImageService.svc/ImageService/Articleimage/2008/LC/b711887b/b711887b-f3.gif>
- <http://aberdeenc.files.wordpress.com/2013/04/finally-done.jpg>



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