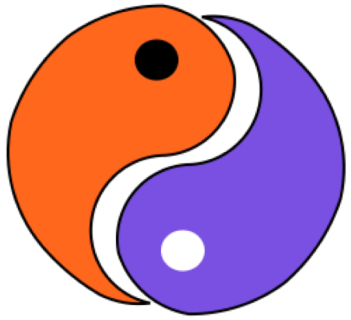
VIRUS & CANCER

Enjeux et perspectives

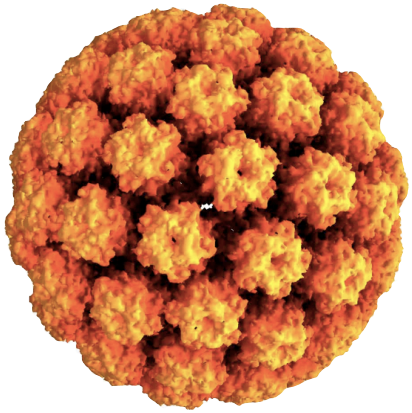
Le Yin et le Yang de la réponse immunitaire dans les lésions induites par les papillomavirus humains.



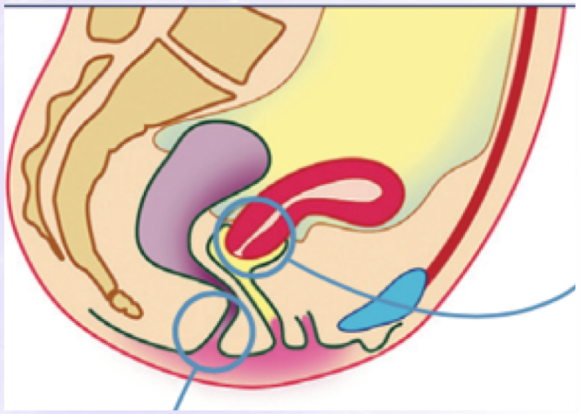
Nathalie Jacobs

Université de Liège

Papillomavirus humain (HPV) et cancers

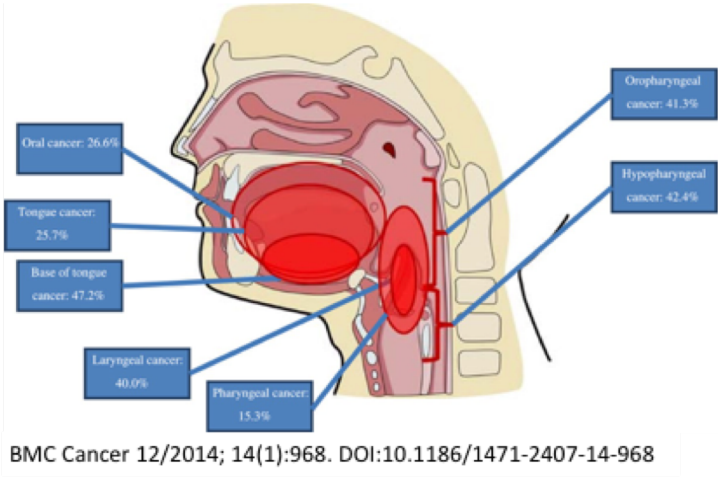


Modis et al, 2002



Herfs et a, Trends in microbiology 2011

Cancer du col de l'utérus



BMC Cancer 12/2014; 14(1):968. DOI:10.1186/1471-2407-14-968

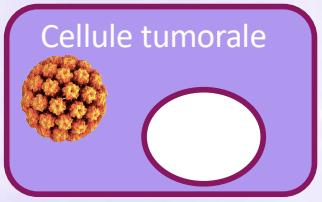
Cancer anal

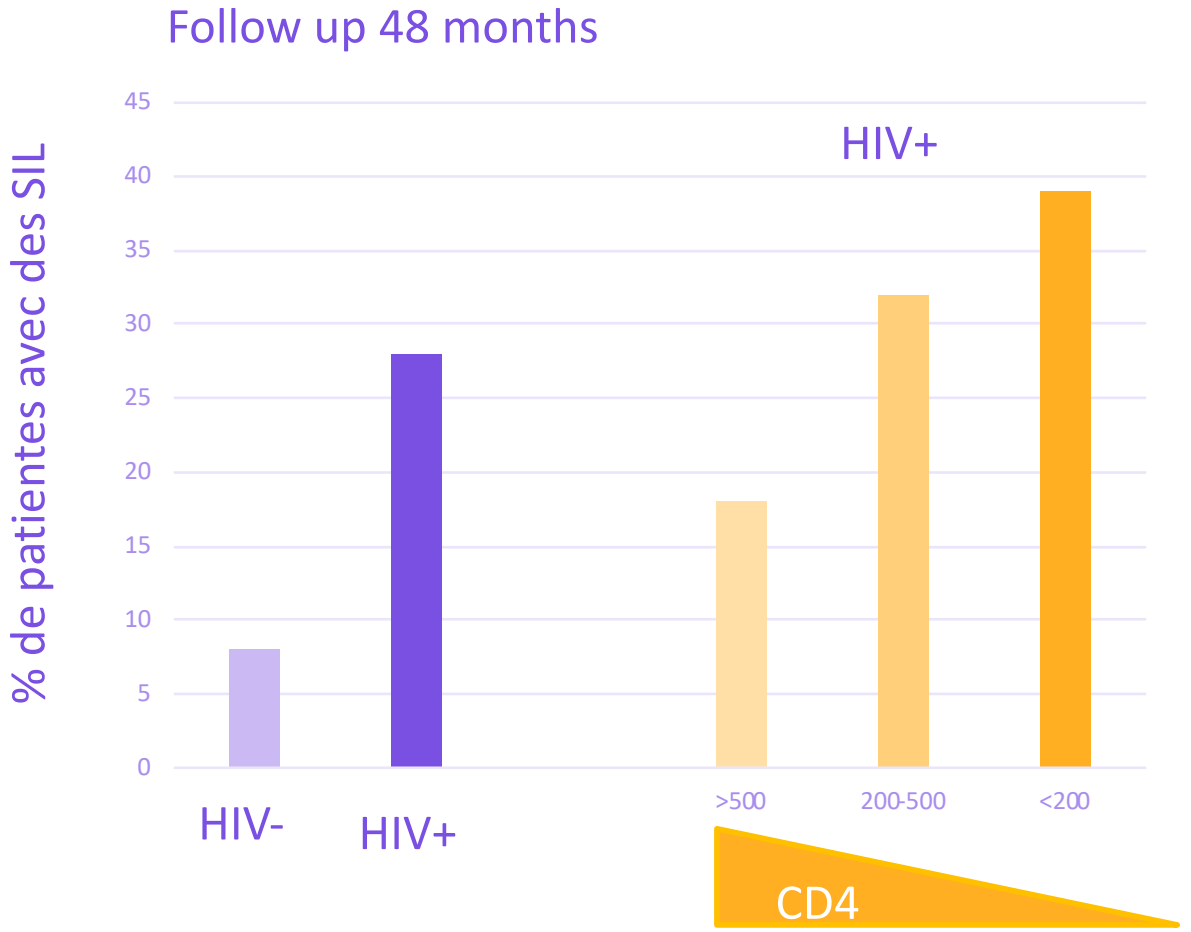
Cancer de la sphère ORL

Lésions pré-néoplasiques (SIL/CIN) bien caractérisées
Absence de production de particules virales dans les cancers

Réponse immunitaire anti-virale/anti-tumorale

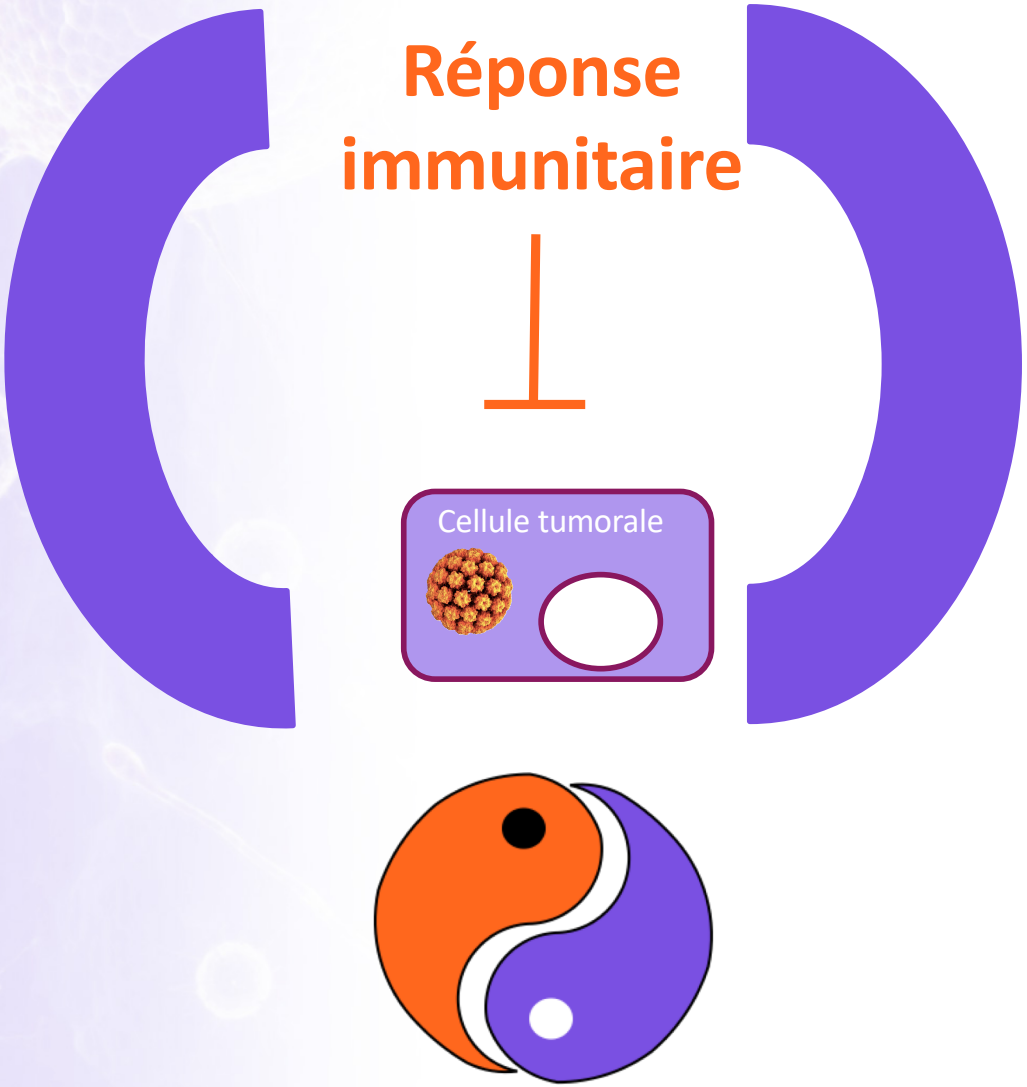
Réponse immunitaire





Adapté de Ellerbrock et al, 2000

Régulation de la réponse immunitaire



Checkpoint inhibitors:
Anti-CTLA-4
Anti-PD1/L1

Lésions HPV

VIRUS & CANCER
Enjeux et perspectives

Published OnlineFirst July 27, 2018; DOI: 10.1158/0008-5472.CAN-18-0892

Tumor Biology and Immunology

Cancer Research

Mucosal HPV E6/E7 Peptide Vaccination in Combination with Immune Checkpoint Modulation Induces Regression of HPV+ Oral Cancers

Stephanie Dorta-Estremera[1], Renee L. Chin[1], Gloria Sierra[1,2], Courtney Nicholas[1], Ananta V. Yanamandra[1], Sita M.K. Nookala[1], Guojun Yang[3], Shail Singh[4], Michael A. Curran[1,2], and K. Jagannadha Sastry[1,2]

NIH U.S. National Library of Medicine
ClinicalTrials.gov

Find Studies | About Studies | Submit Studies | Resources | About Site

Home > Search Results > Study Record Detail

Save this study

Ipilimumab, Nivolumab, and Radiation Therapy in Treating Patients With HPV Positive Advanced Oropharyngeal Squamous Cell Carcinoma

Anti-CTLA4 et anti-PD1

The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. Know the risks and potential benefits of clinical studies and talk to your health care provider before participating. Read our disclaimer for details.

ClinicalTrials.gov Identifier: NCT03799445

Recruitment Status : Not yet recruiting
First Posted : January 10, 2019
Last Update Posted : June 13, 2019

See Contacts and Locations

INNATE-ADAPTIVE RESPONSE

Checkpoint inhibitors
(anti-CTLA4 et PD1-PDL1)

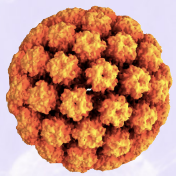
Adaptive immunity
T and B lymphocytes

Innate lymphoid cells (ILC)

Natural Killer (ILC1), ILC2… and **γδ T cells**

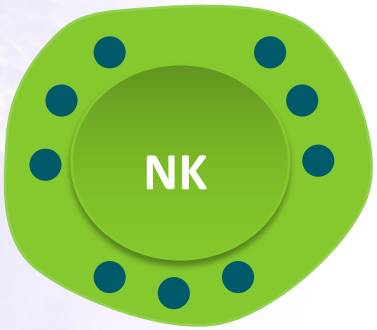
Innate immunity
antimicrobial peptides, complements,
granulocytes, dendritic cells, macrophages

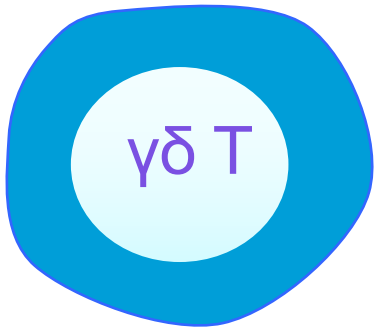
Time



complexity

NK cells and γδ T cells





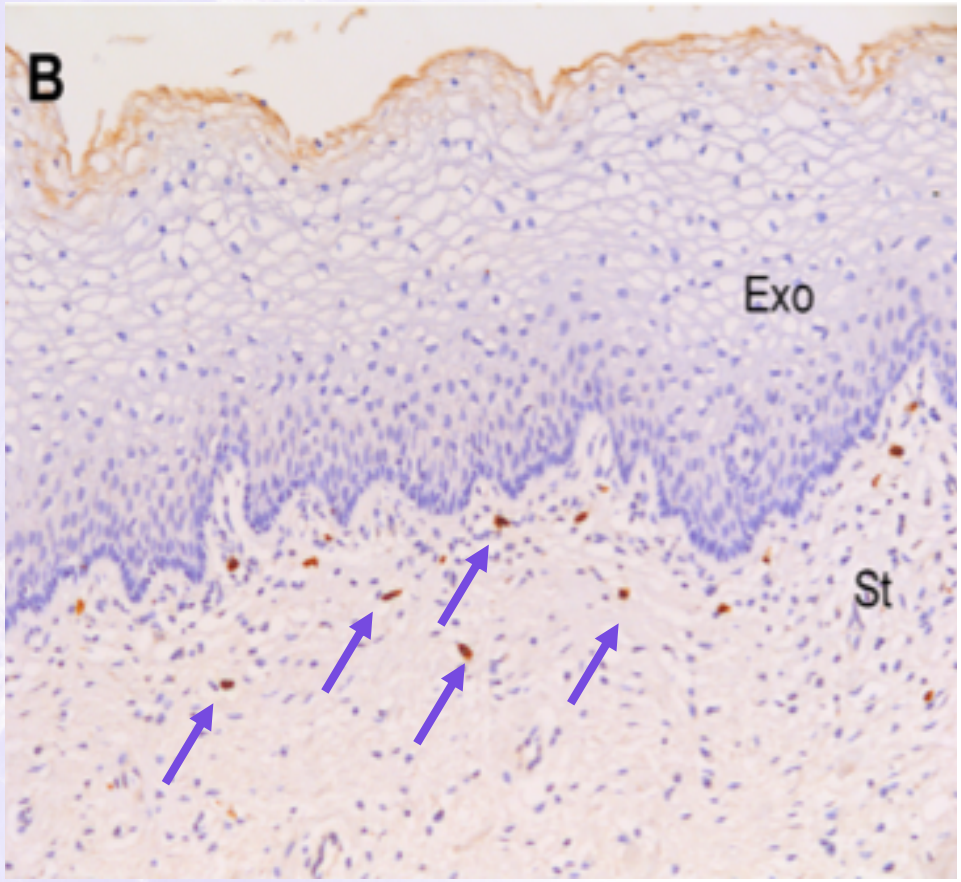
Role in anti-viral and anti-tumoral responses

Killer cells
Production of IFN-γ

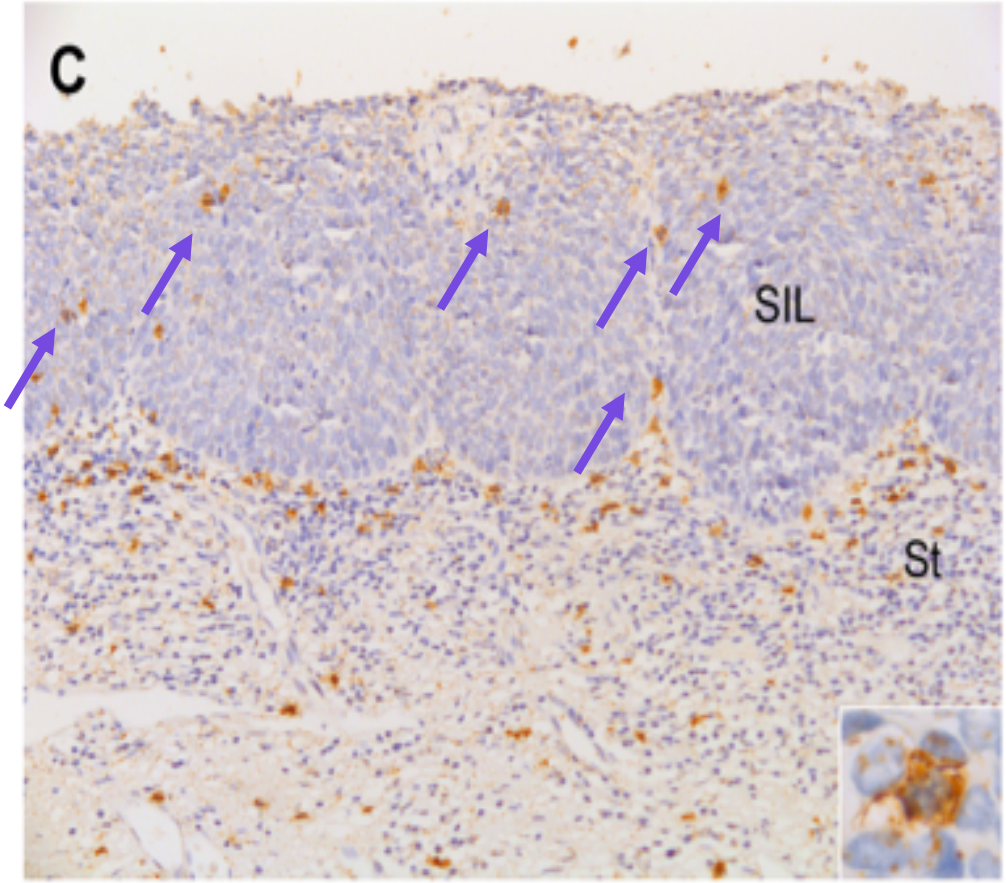
Malkosky et al, 2001; Veuillen et al, 2009; Raulet et al, 2013;
Norell et al, 2013

NK cell infiltration in HPV-associated lesions

NK (NKP46) staining normal exocervix



NK (NKP46) staining SIL

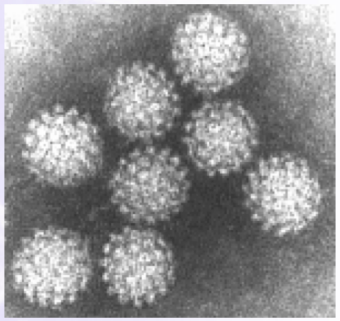


Renoux et al, Eur J Immunol 2011

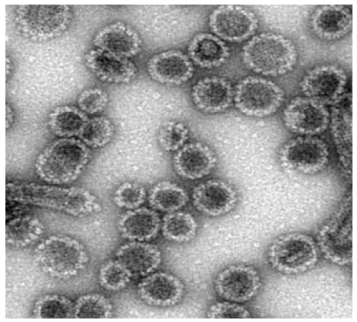
Direct interaction with the virus?

HPV: model...

No virus available



Use of virus-like particles (VLP)

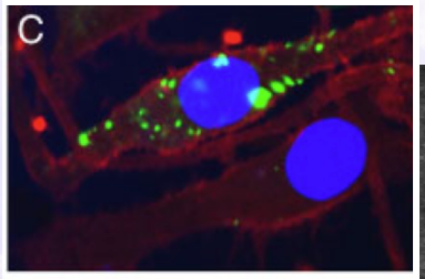


L1 protein assembly

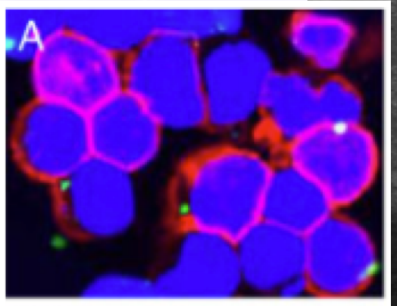
Vaccine Ag

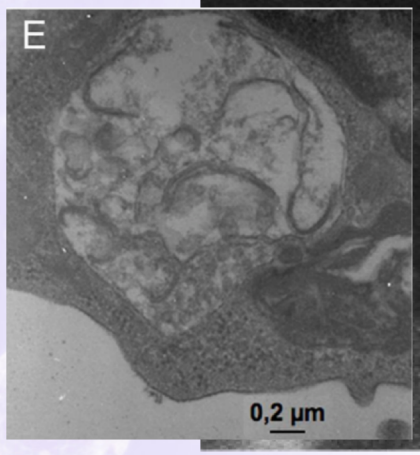
Human papillomavirus entry into NK cells requires CD16 expression and triggers cytotoxic activity and cytokine secretion

Kératinocytes



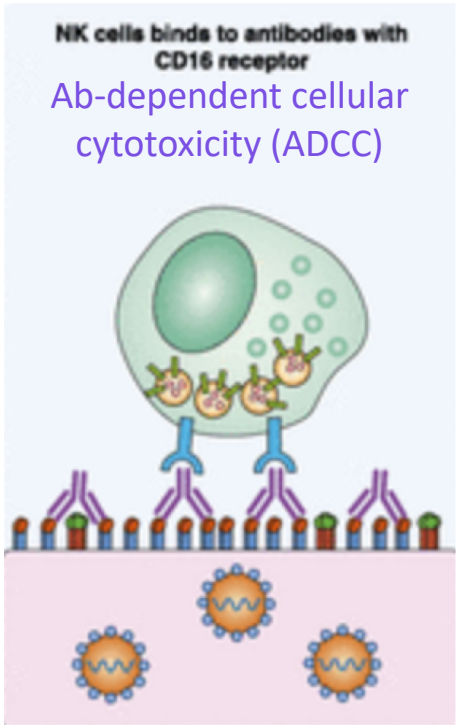
Cellules NK





VLP-HPV

CD16

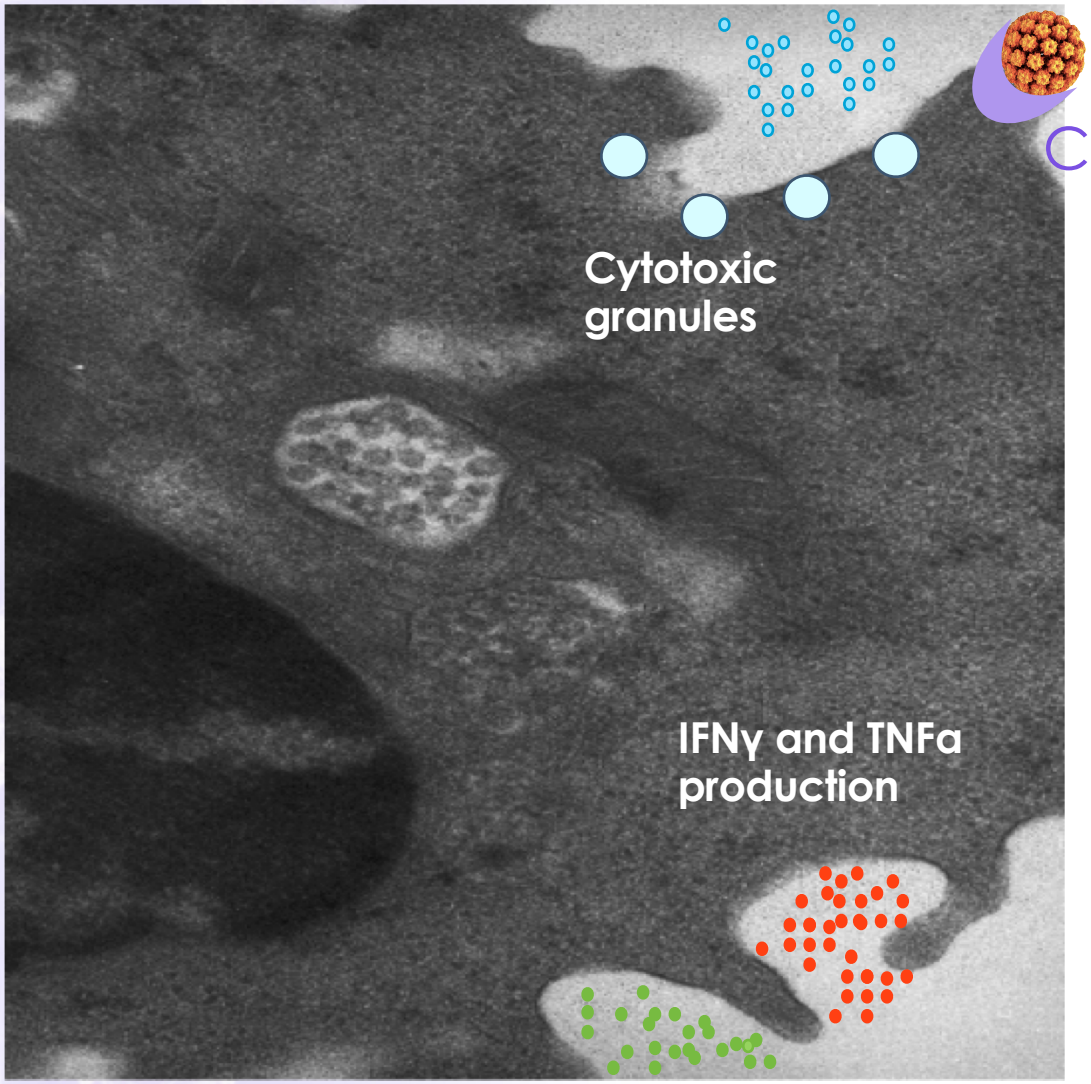


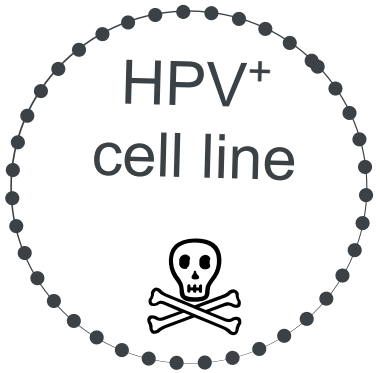
Ab-dependent cellular cytotoxicity (ADCC)

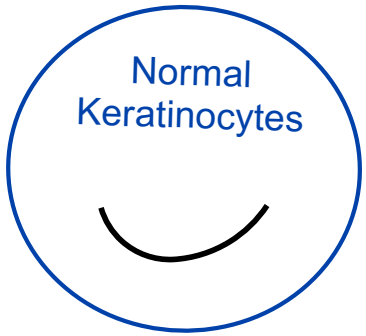
Jegaskanda et al, JI 2014

Renoux et al, Eur J Immunol 2011

Human papillomavirus entry into NK cells requires CD16 expression and triggers cytotoxic activity and cytokine secretion

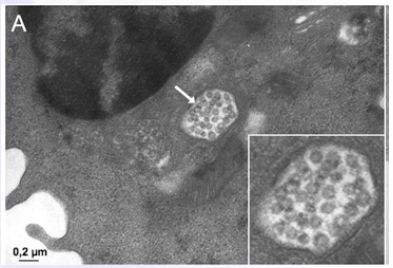


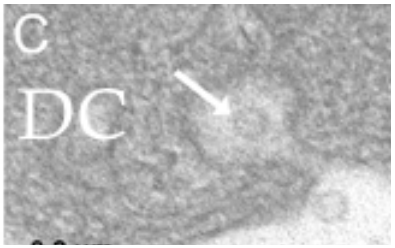


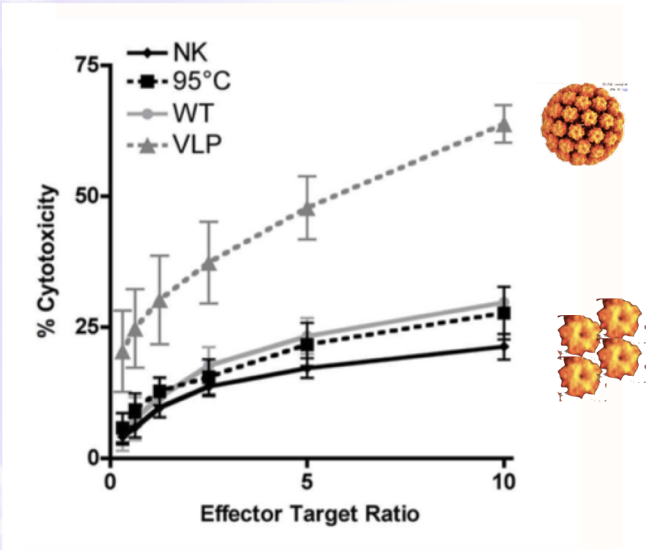


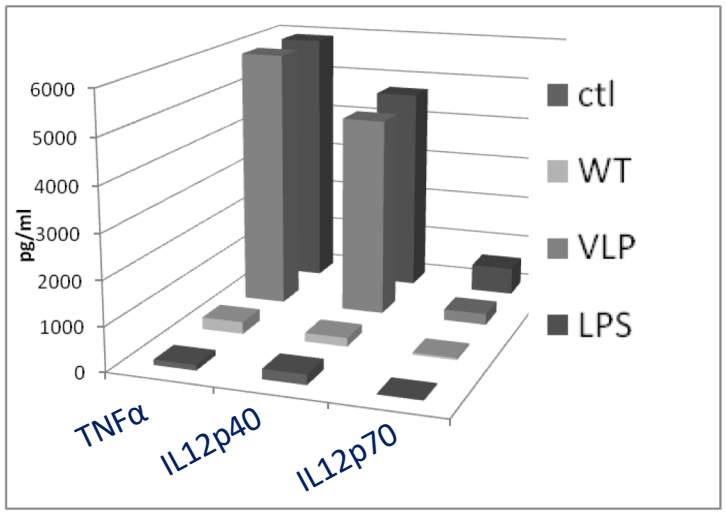
Renoux et al, Eur J Immunol 2011

NK-DC collaboration in presence of HPV-VLP?





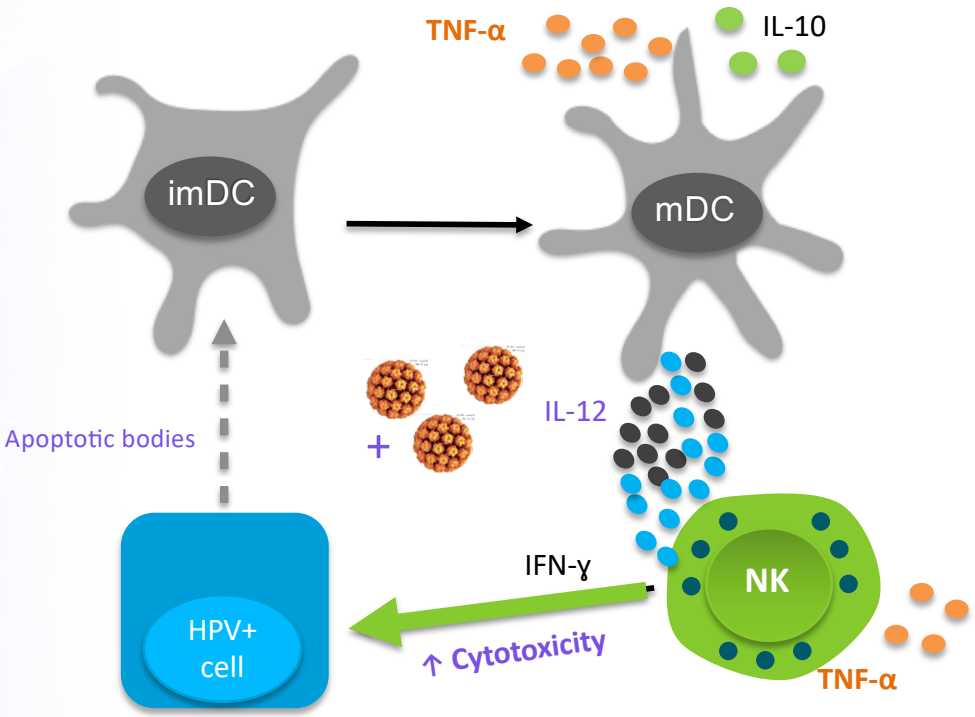




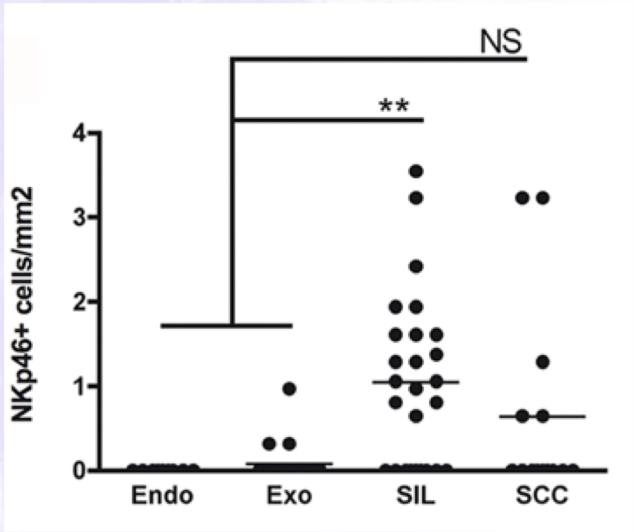
Natural killer and dendritic cells collaborate in the immune response induced by the vaccine against uterine cervical cancer

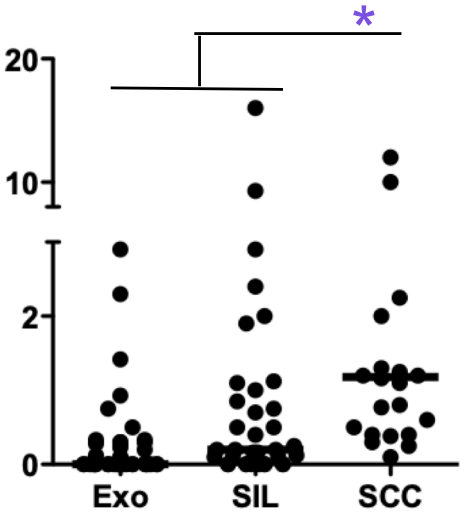
Inge Langers[1], Virginie Renoux[1], Anca Reschner[2], Antoine Touzé[3], Pierre Coursaget[4], Jacques Boniver[2], Joachim Koch[5], Philippe Delvenne[2] and Nathalie Jacobs[1]

Eur. J. Immunol. 2014. 44: 3585–3595

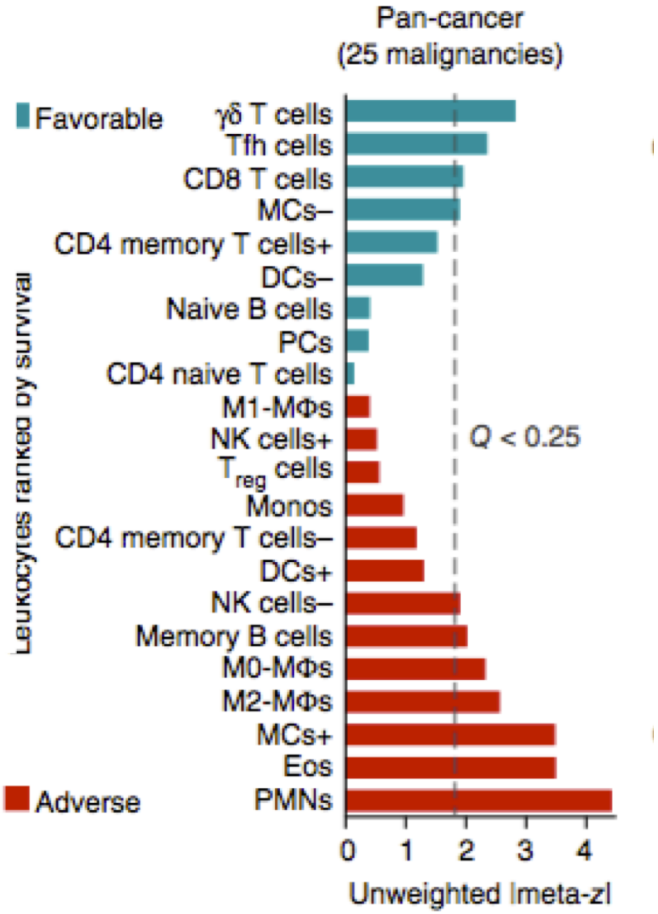


NK and γδ T cell infiltration in HPV-associated lesions





Global prognostic associations for 22 leukocyte types

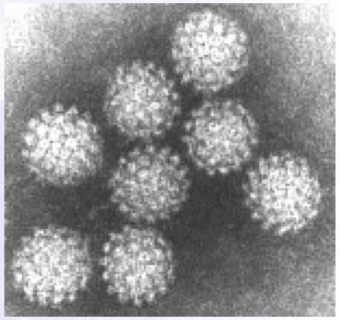


Gentles AJ et al, Nature Med August 2015

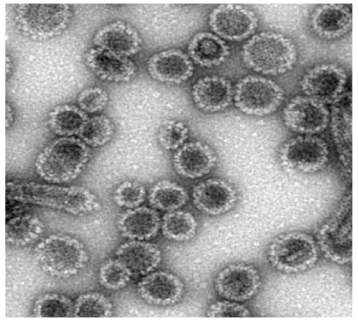
HPV: models...

VIRUS & CANCER
Enjeux et perspectives

No virus available



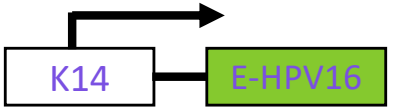
Use of virus-like particles (VLP)



L1 protein assembly

Until recently no murine papillomavirus infection model

Transgenic mouse model



Arbeit et al, 1994

Murine papillomavirus (MmuPV1) in 2011

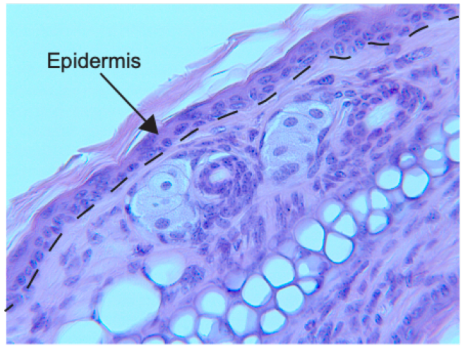
A Novel *In Vivo* Infection Model To Study Papillomavirus-Mediated Disease of the Female Reproductive Tract

Megan E. Spurgeon,[a] Aayushi Uberoi,[a]* Stephanie M. McGregor,[b] Tao Wei,[a] Ella Ward-Shaw,[a] Paul F. Lambert[a]

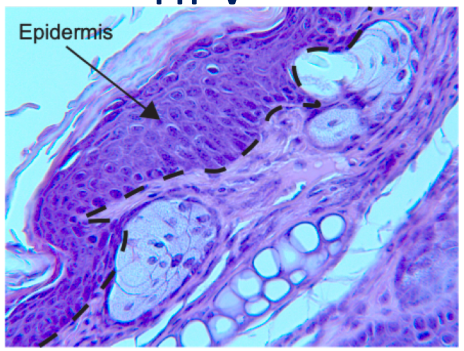
March/April 2019 Volume 10 Issue 2 e00180-19

AMERICAN SOCIETY FOR MICROBIOLOGY | mBio®

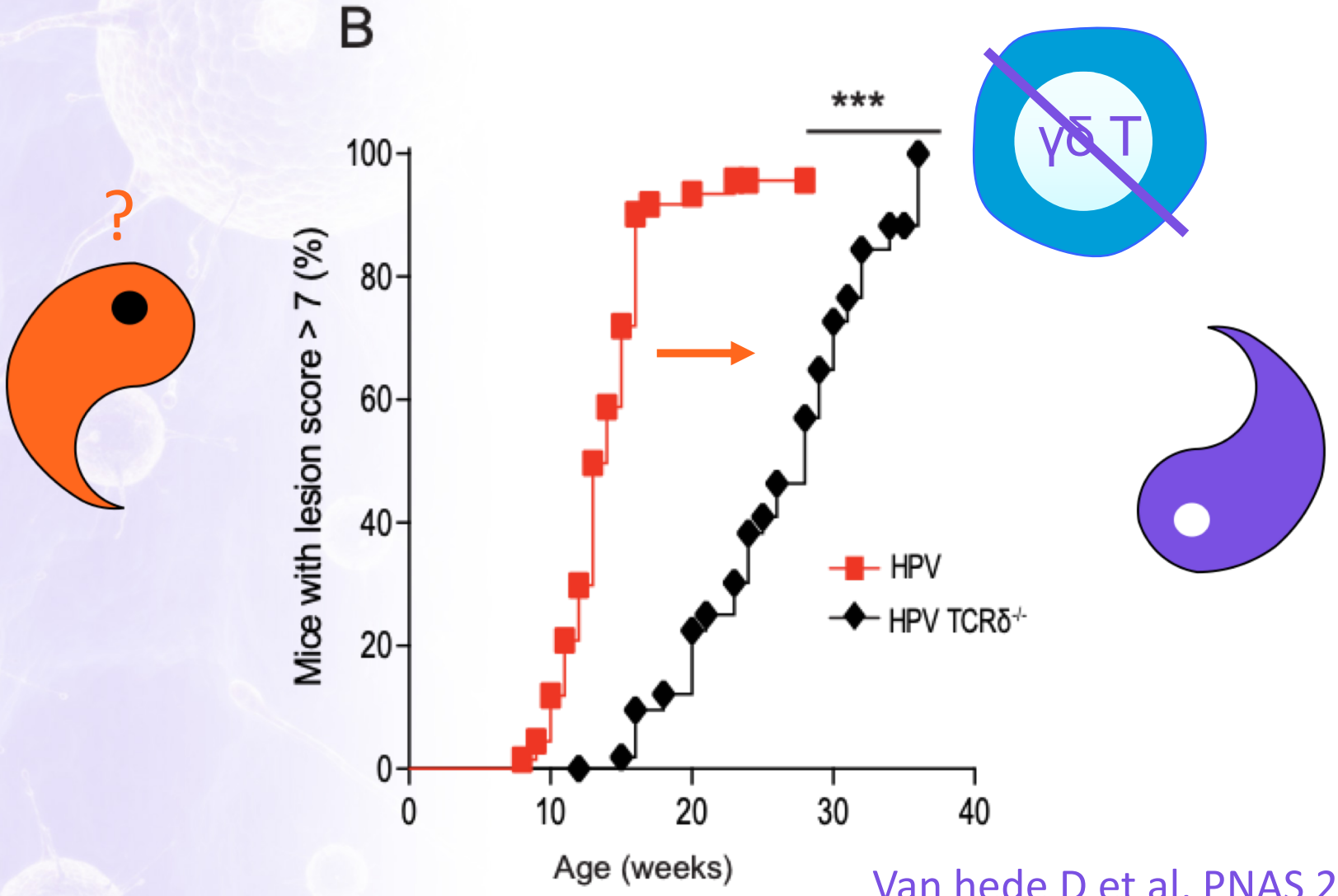
WT



HPV$^{T/-}$



γδ T cells accelerate the development of HPV-induced lesions in the K14-HPV16 mouse model



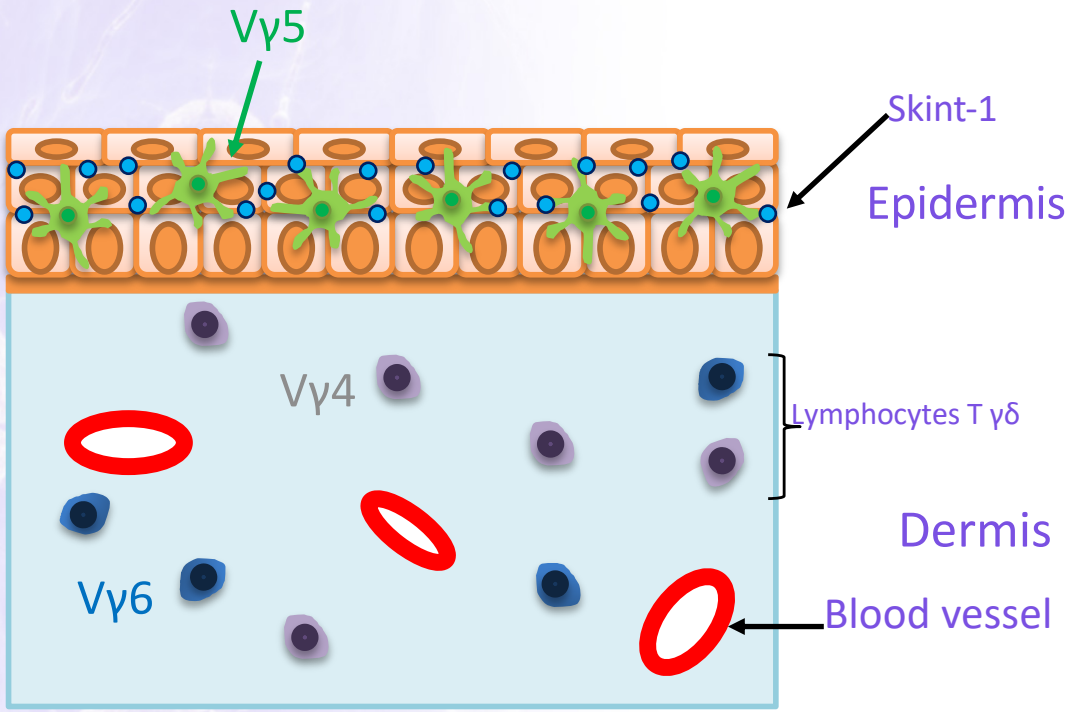
Van hede D et al, PNAS 2017

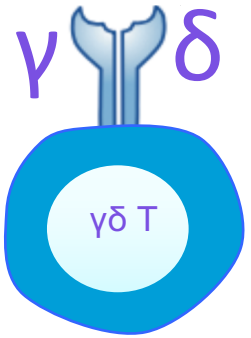
Méchanisme?

Van hede D et al, PNAS 2017

VIRUS & CANCER
Enjeux et perspectives

WT mouse



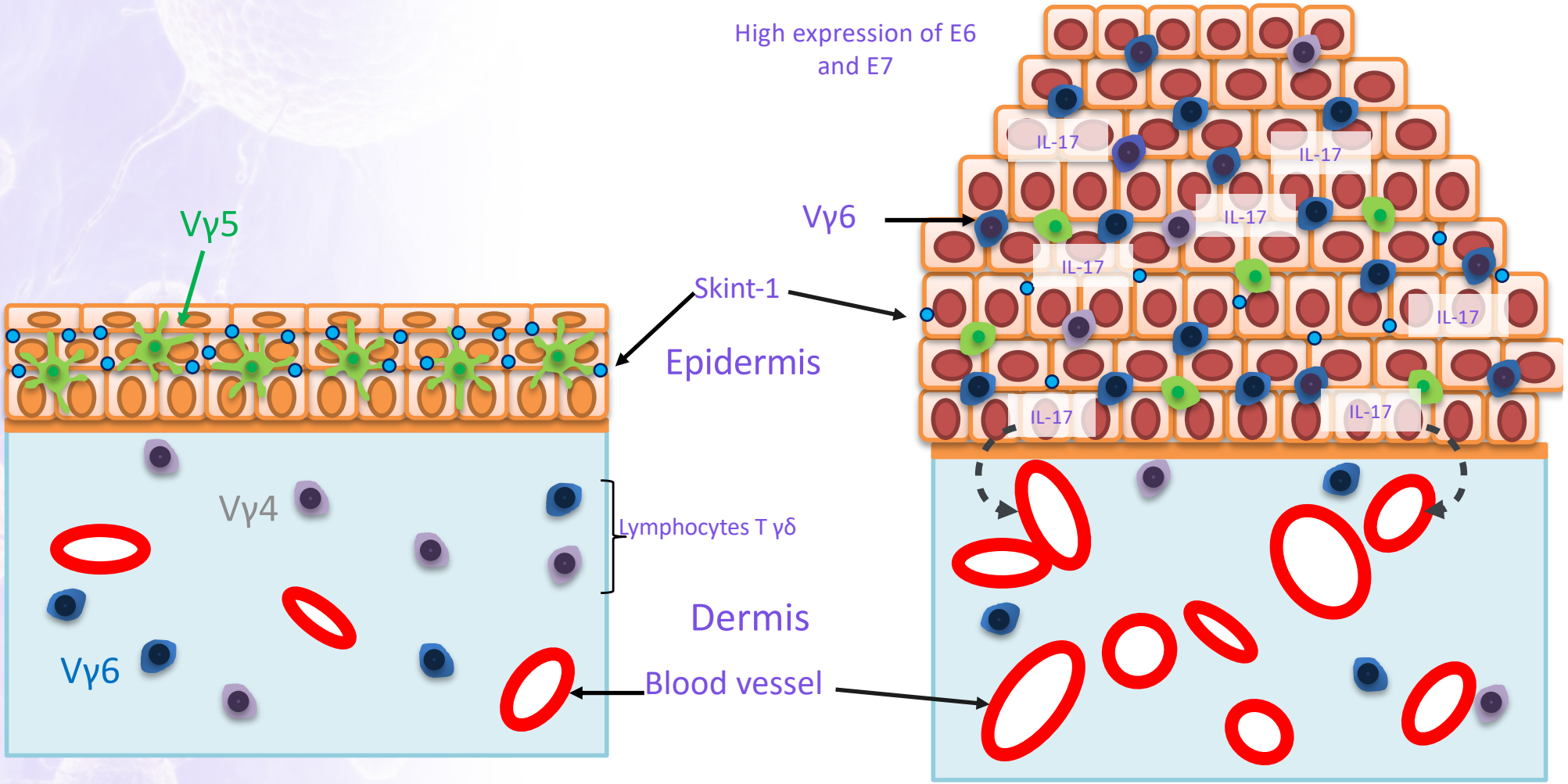


Méchanisme?

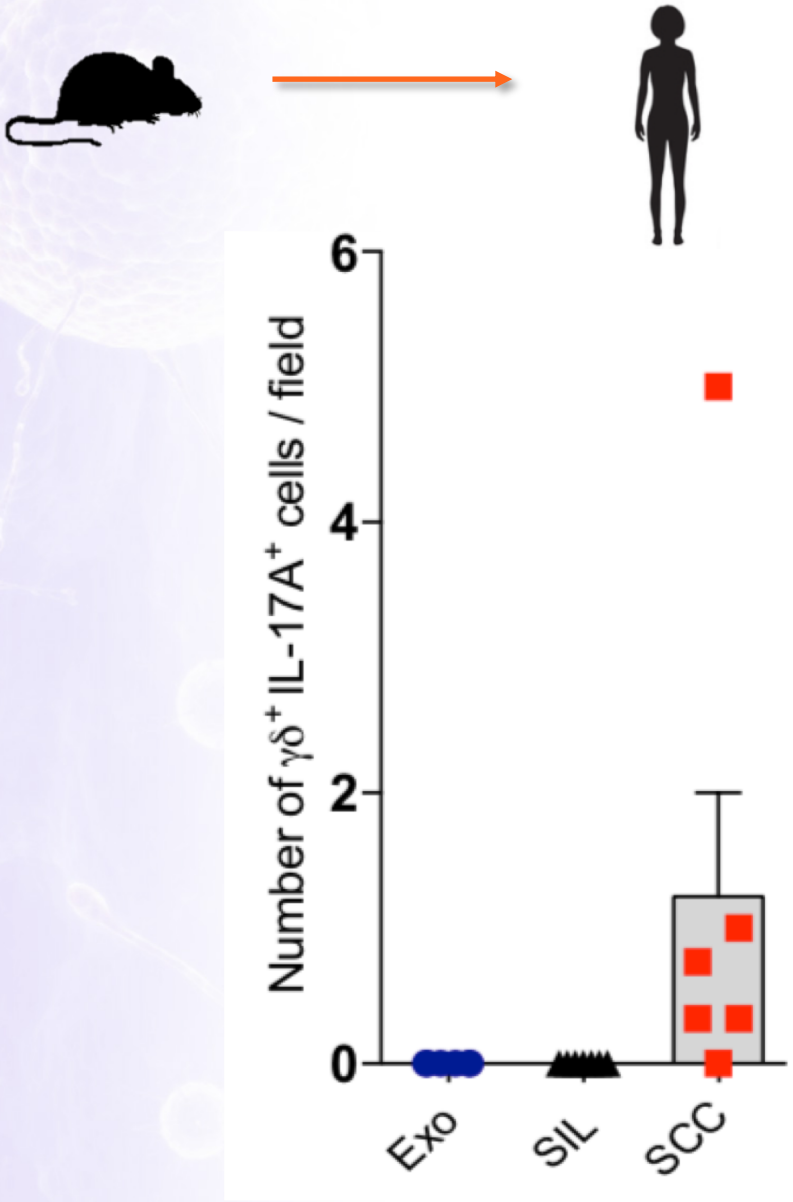
Van hede D et al, PNAS 2017

WT mouse

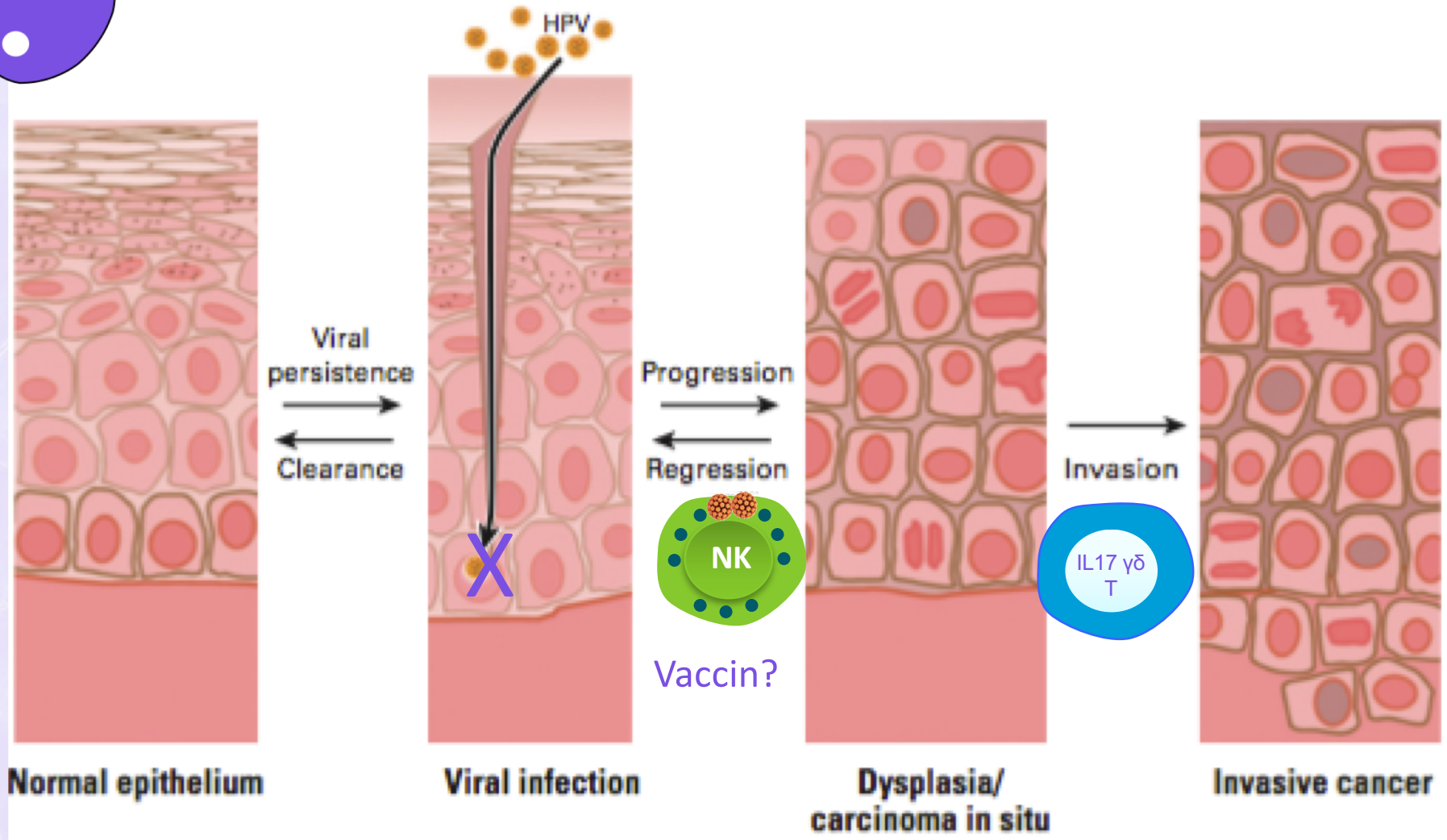
HPV mouse



Human cervical squamous cell carcinoma (SCC) contains IL-17A producing γδ T cells.



NK cells and γδ T cells in HPV lesions



Adapted from K Hellner and K Munger, 2011