

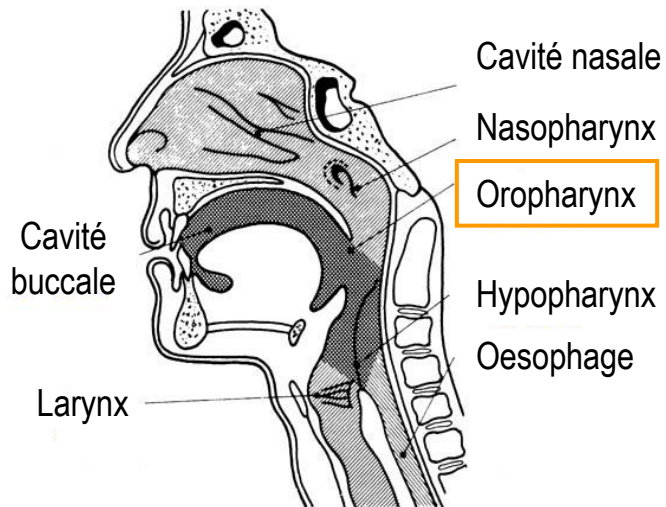
A novel Δ Np63-dependent immune mechanism improves prognosis of HPV-related head and neck cancer

Dr Alain JUNG
Laboratoire de Biologie Tumorale
Institut de Cancérologie Strasbourg Europe

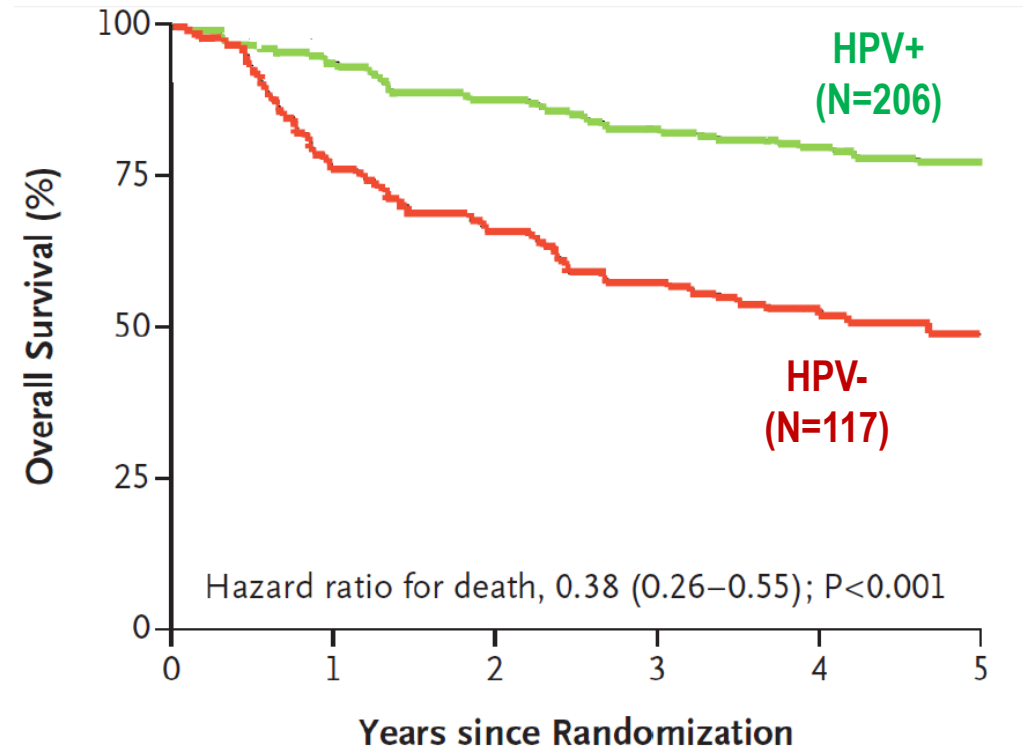
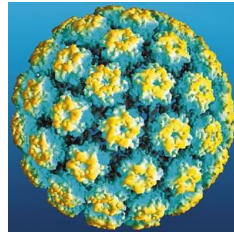
13^{ème} Forum du Cancéropole Est
Strasbourg - 10 Novembre 2023

CANCERS OROPHARYNGES HPV-POSITIFS

- **>50%** des cancers oropharyngés
- Type viral **HPV16 majoritaire** (>80-90% des cas)
- **Incidence** OSCC HPV+ en **augmentation**
- **Pronostic** > HPV-négatifs
- Statut HPV inclus dans **8^{ème} édition AJCC staging**

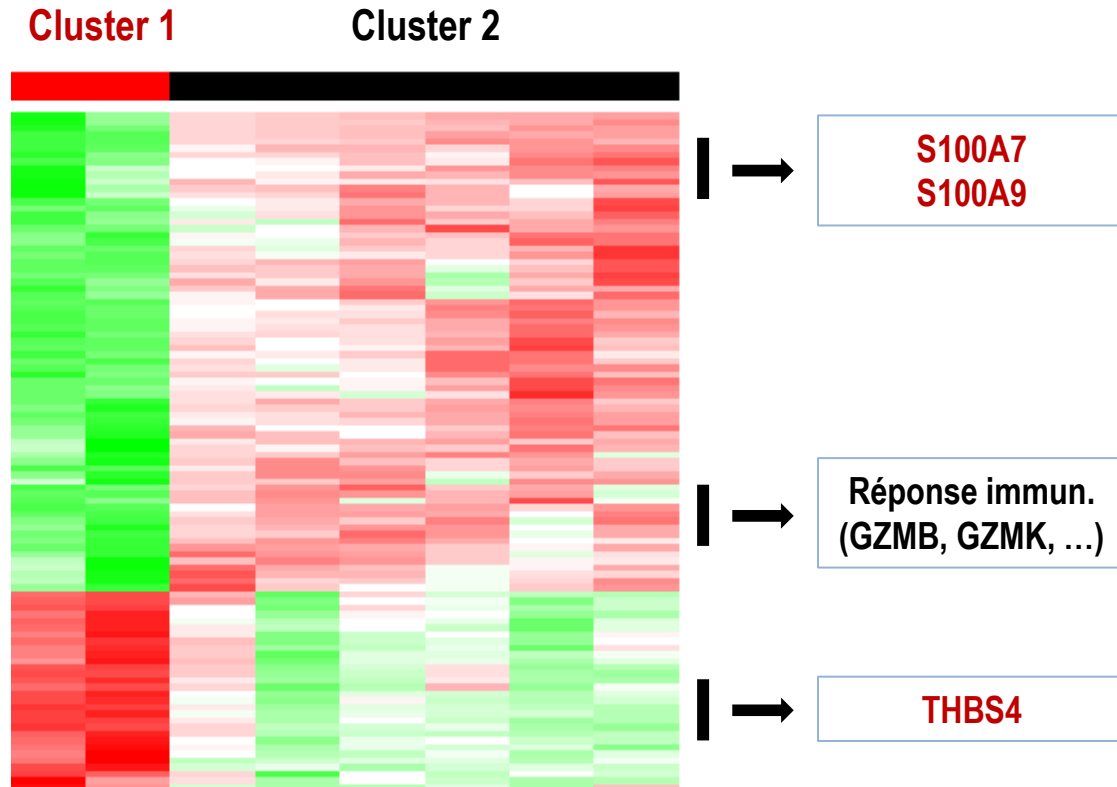


Human Papillomavirus (HPV)

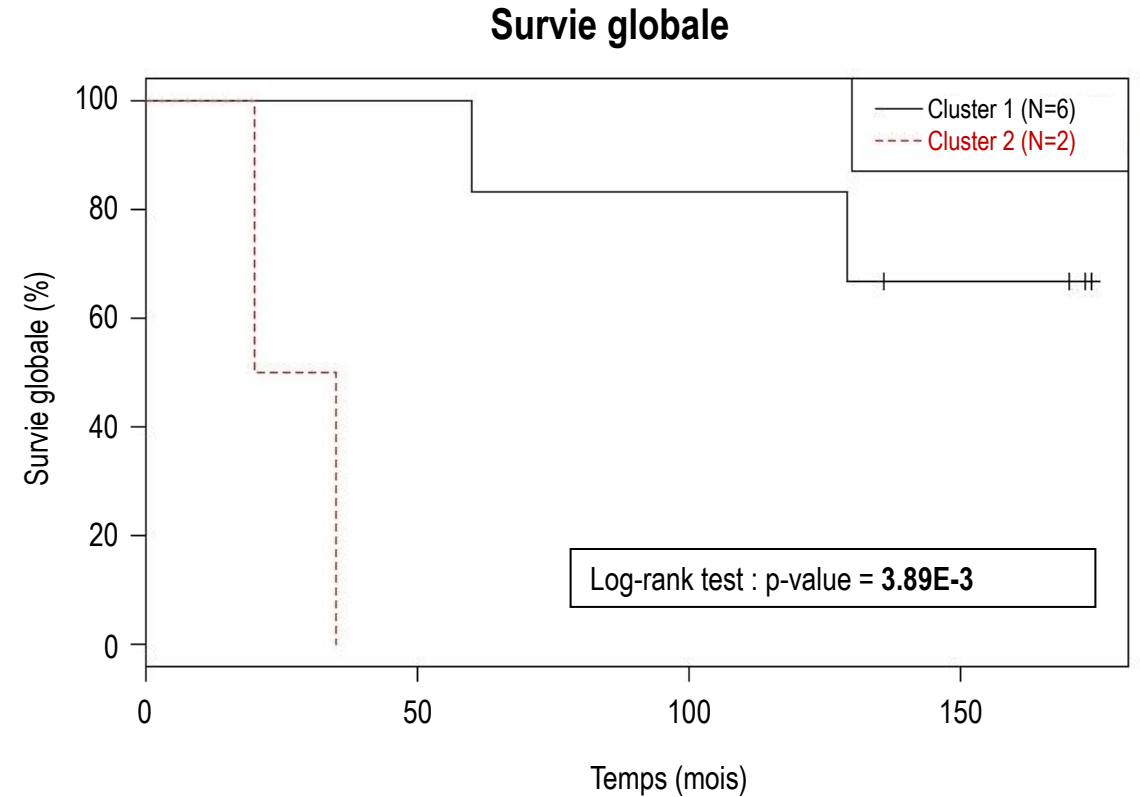


D'après Ang et al., 2010

HÉTÉROGÉNÉITÉ MOLÉCULAIRE DES TUMEURS OROPHARYNGÉES HPV-POSITIVES

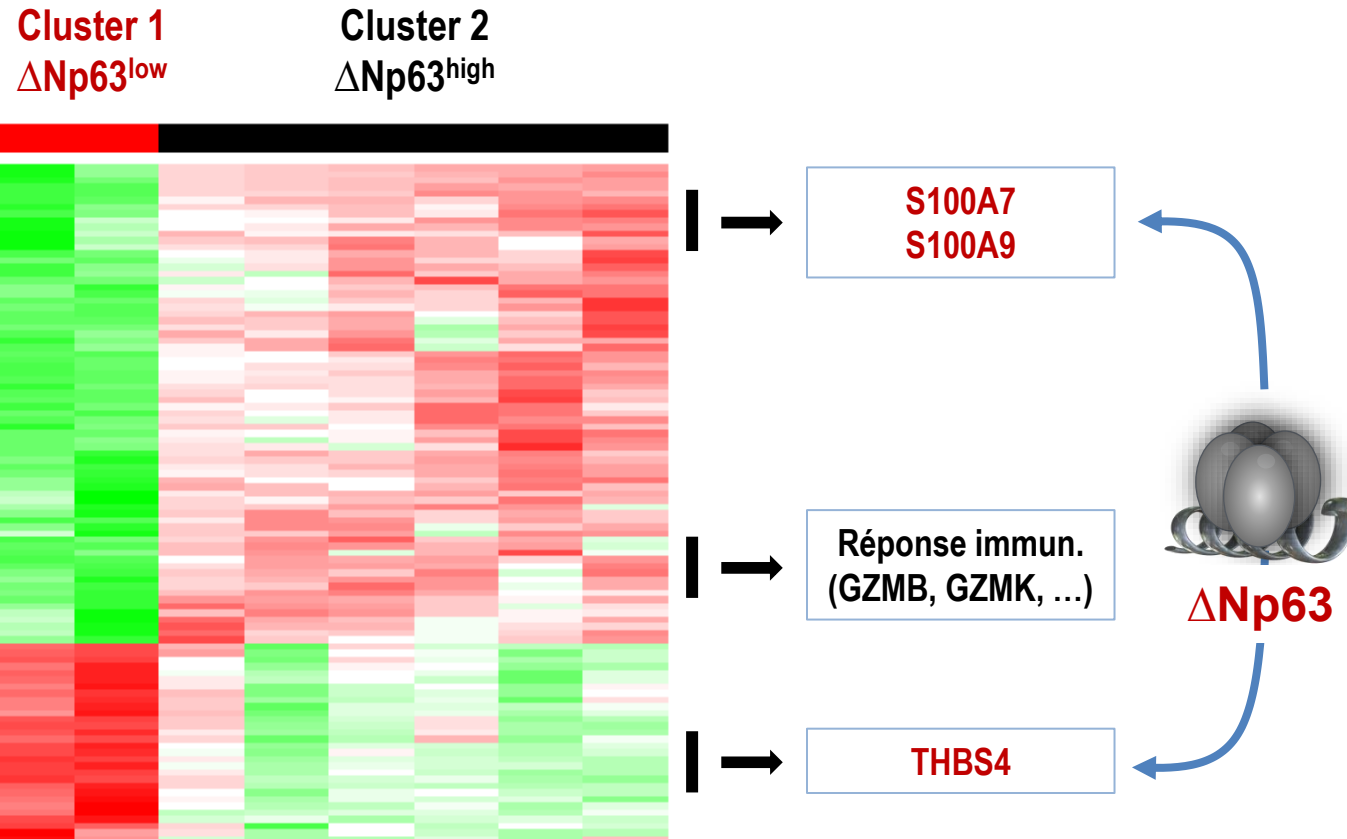


Analyse **non supervisée** de données de **transcriptomique**



Mourtada *et al.*, Front Immunol 2023

HÉTÉROGÉNÉITÉ MOLÉCULAIRE: SIGNATURE DÉPENDANTE DE Δ NP63



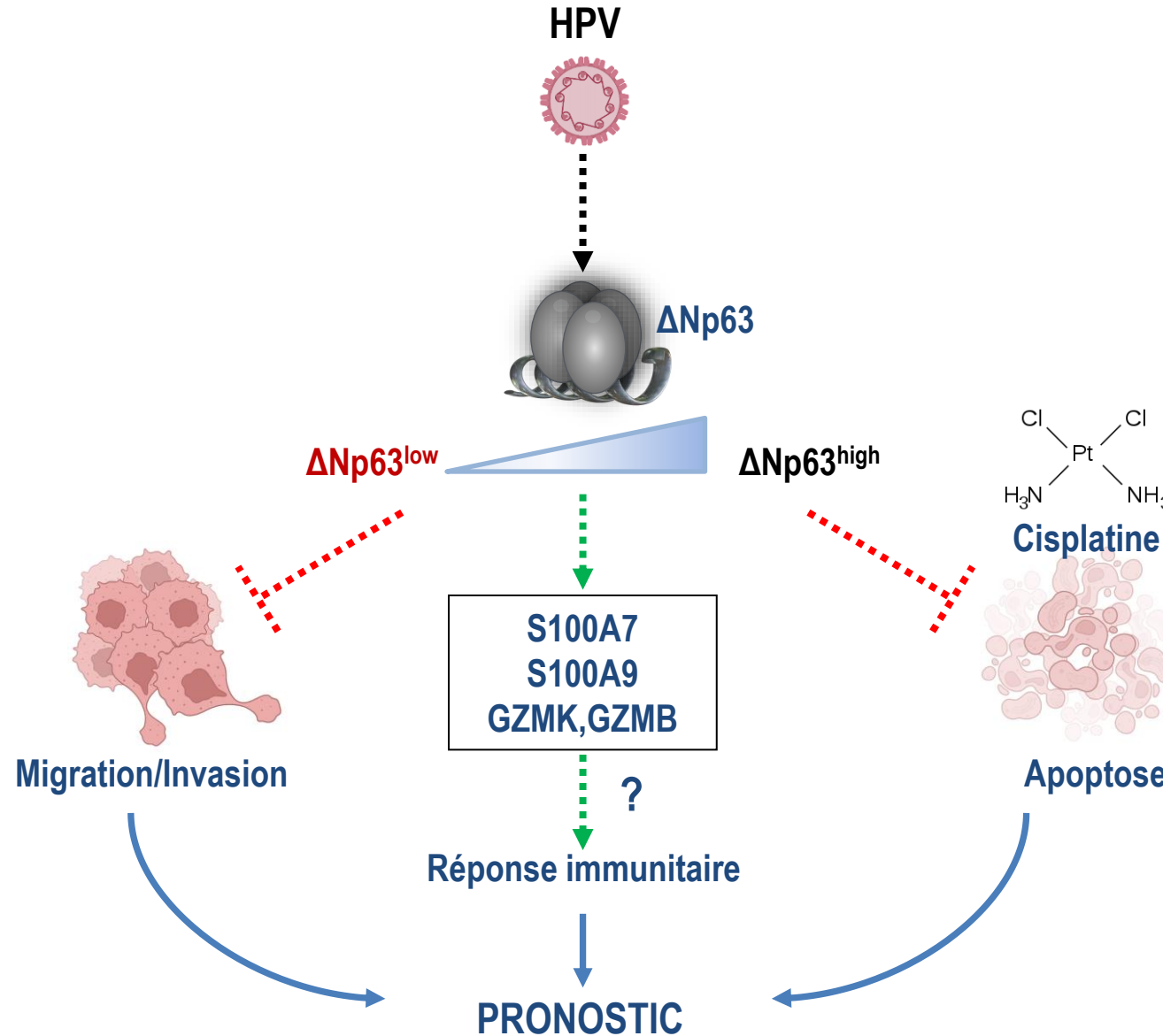
Analyse **non supervisée** de données de **transcriptomique**

Loss of p63 Leads to Increased Cell Migration and Up-regulation of Genes Involved in Invasion and Metastasis

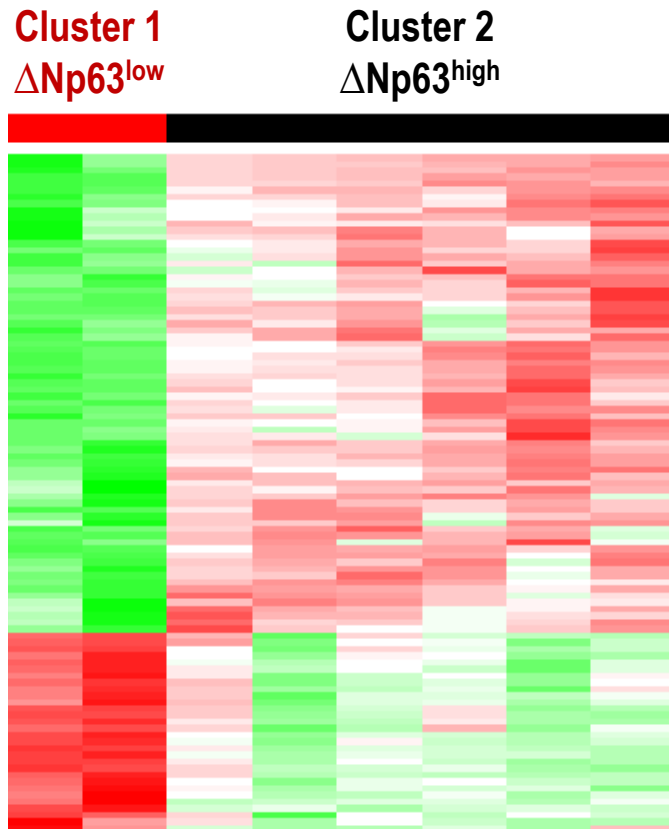
Christopher E. Barbieri,^{1,3} Luo Jia Tang,^{1,3} Kimberly A. Brown,^{2,3} and Jennifer A. Pietenpol^{1,3}
Cancer Res 2006; 66: (15). August 1, 2006

Mourtada *et al.*, Front Immunol 2023

Δ NP63 JOUE UN ROLE DE SUPPRESSEUR DE TUMEUR

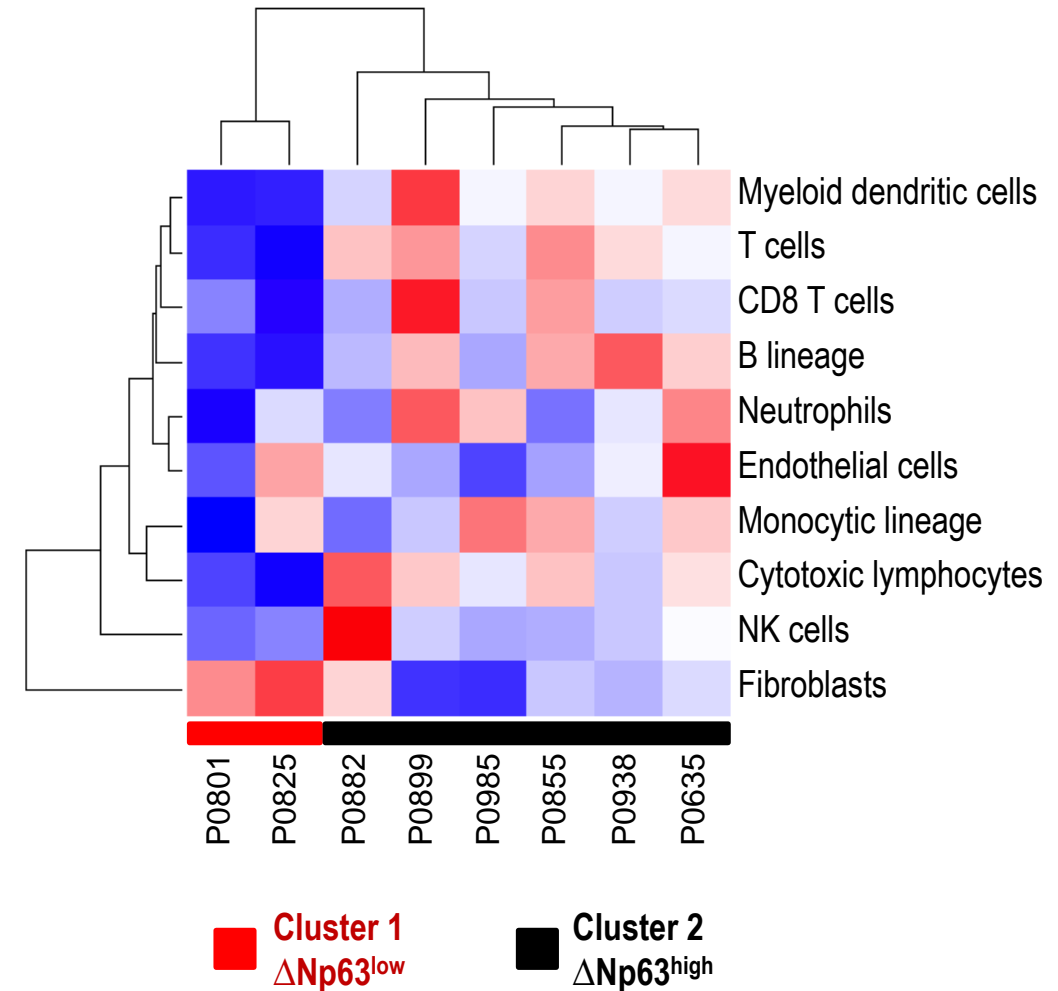


Δ NP63 EST ASSOCIÉ À UNE INFILTRATION DE CELLULES IMMUNITAIRES

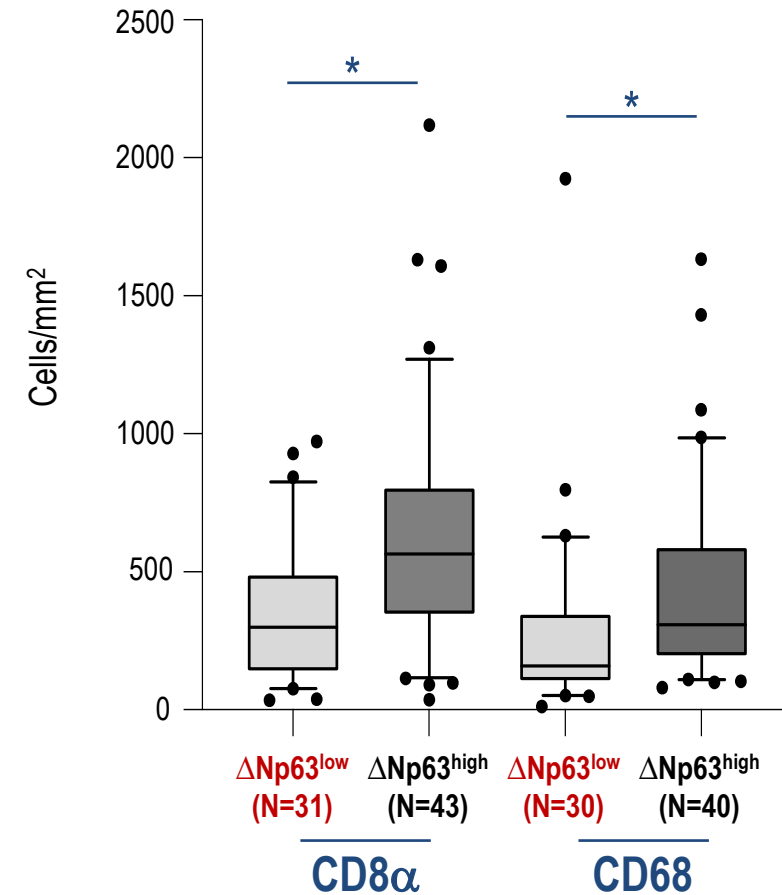
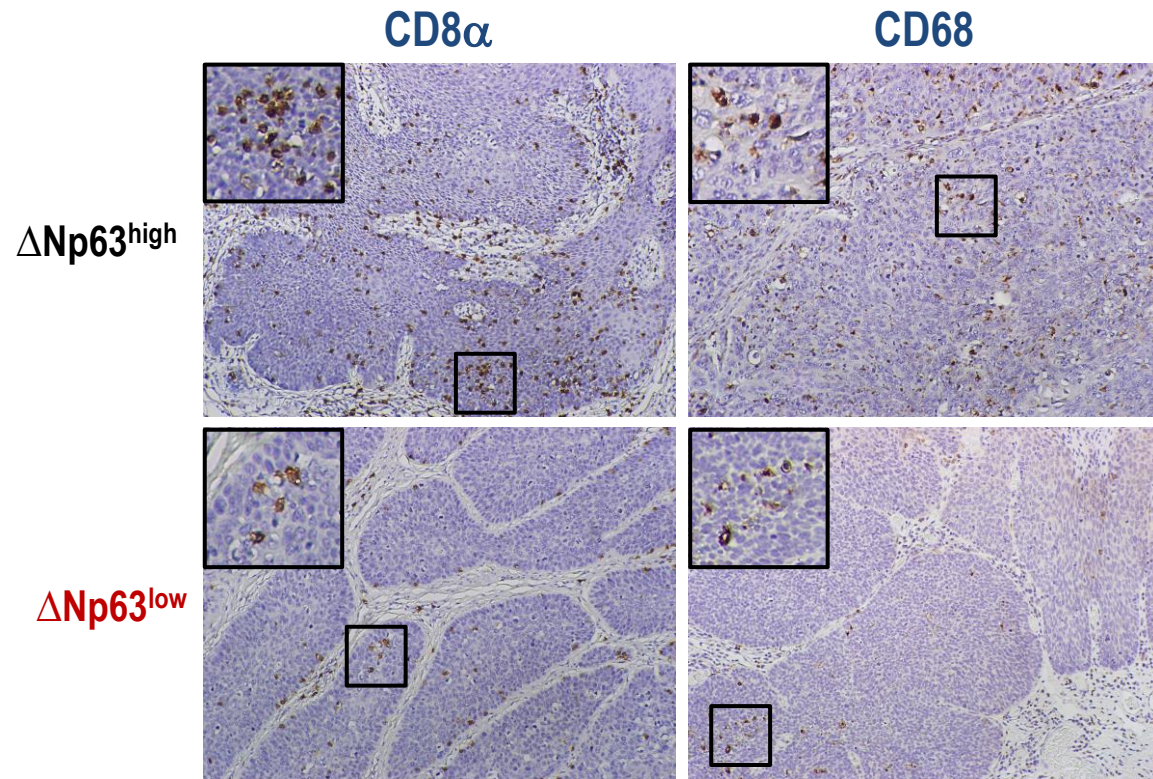


Déconvolution des données transcriptomiques

→

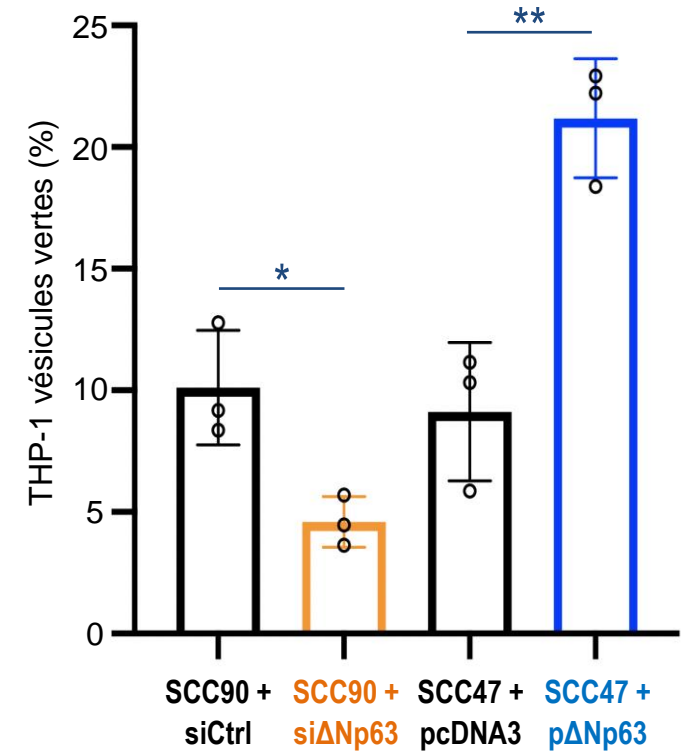
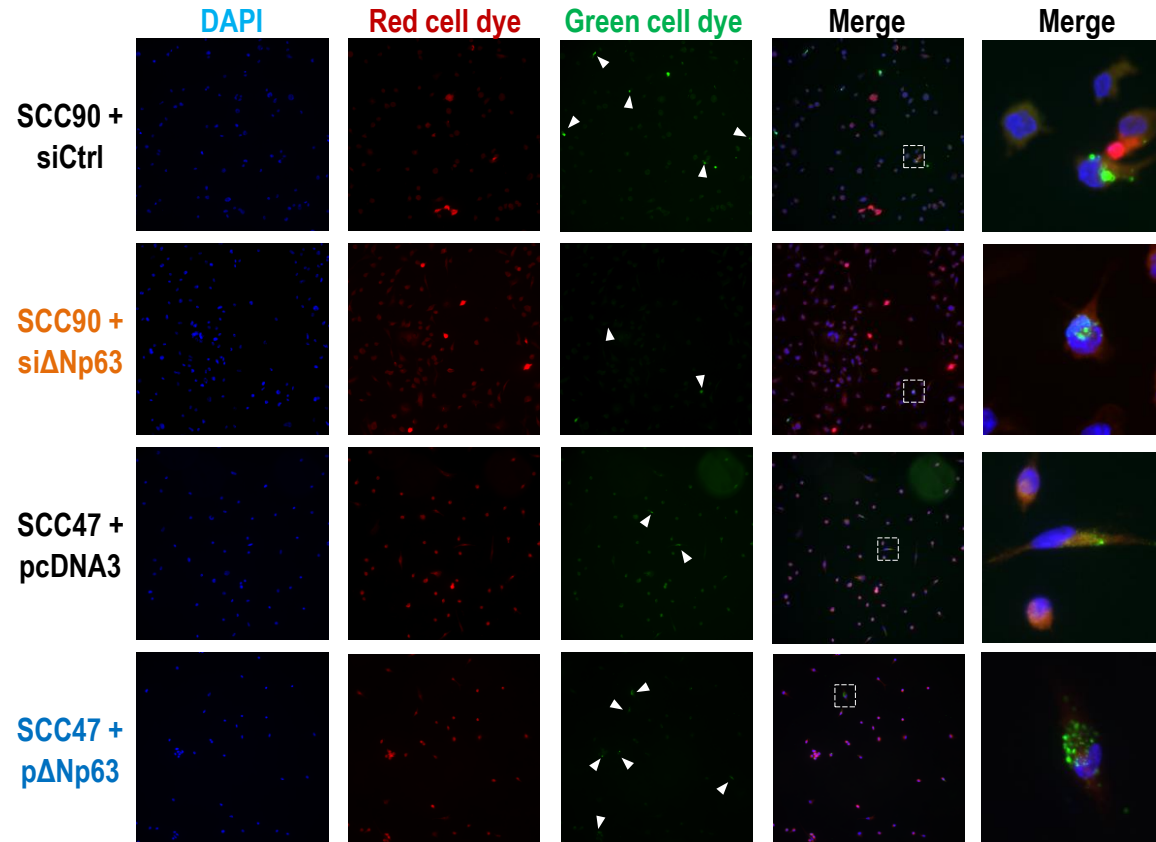
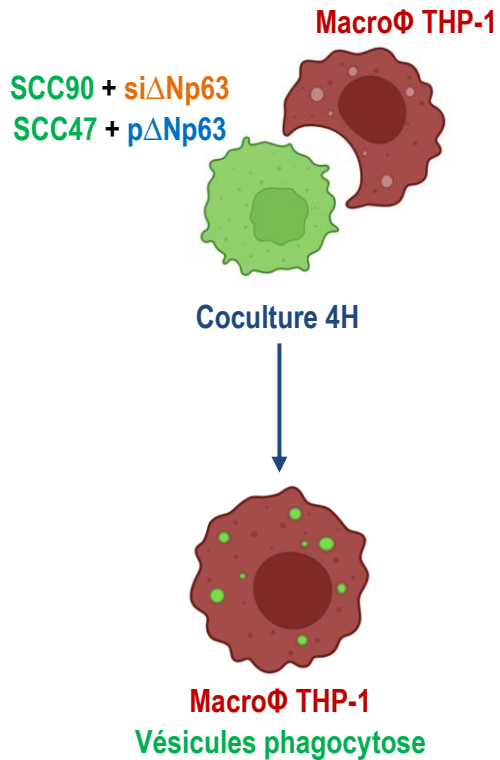


Δ NP63 EST ASSOCIÉ À UNE INFILTRATION DE CELLULES IMMUNITAIRES

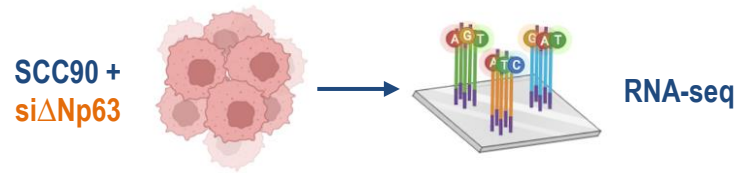


ΔNP63 STIMULE LA PHAGOCYTOSE DES CELLULES CANCÉREUSES

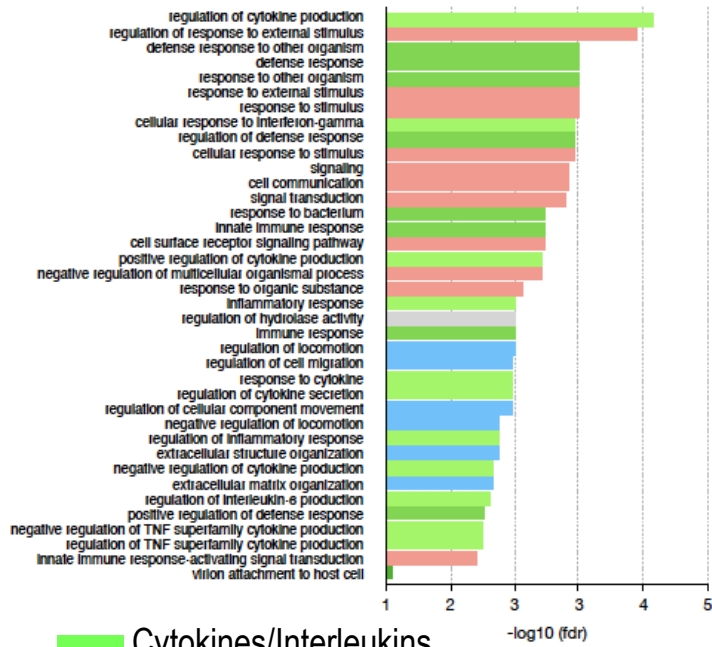
In vitro phagocytosis assay



ΔNP63 CONTROLE L'EXPRESSION DE MOLÉCULES DIFFUSIBLES IMMUNOMODULATRICES

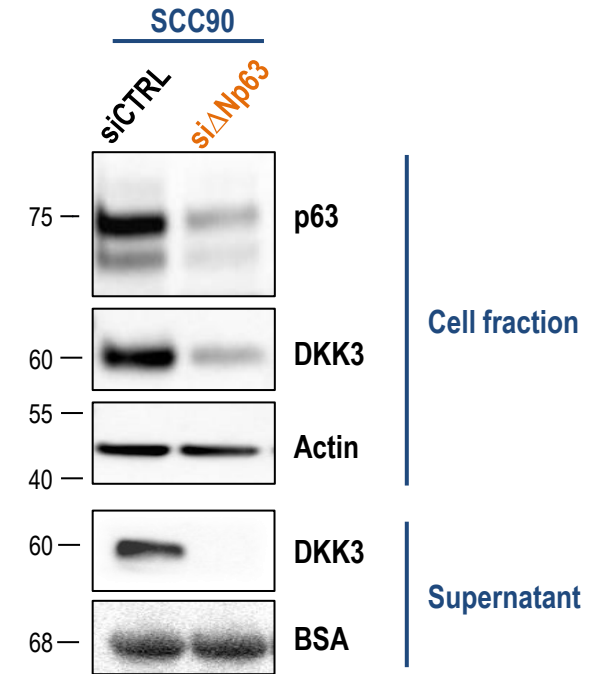
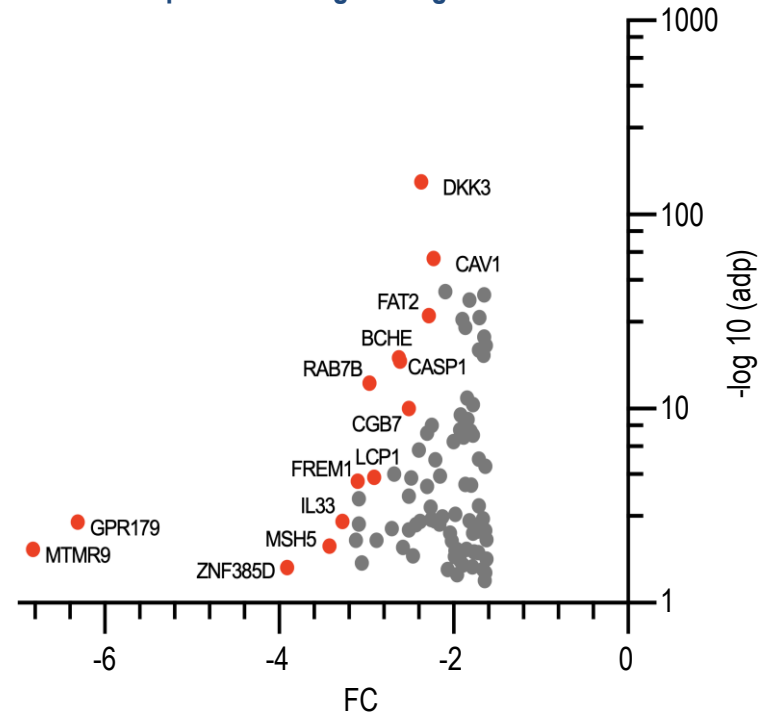


Top downregulated pathways



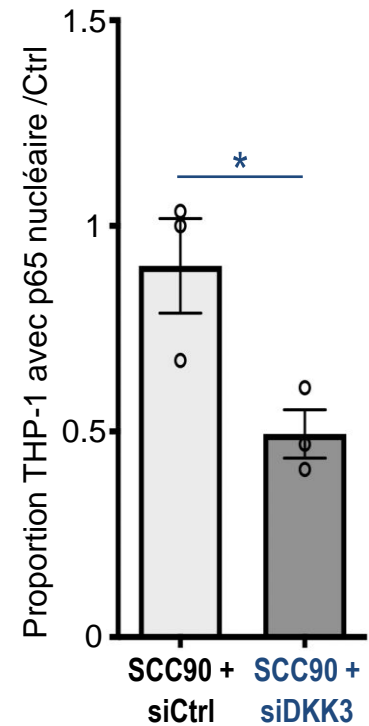
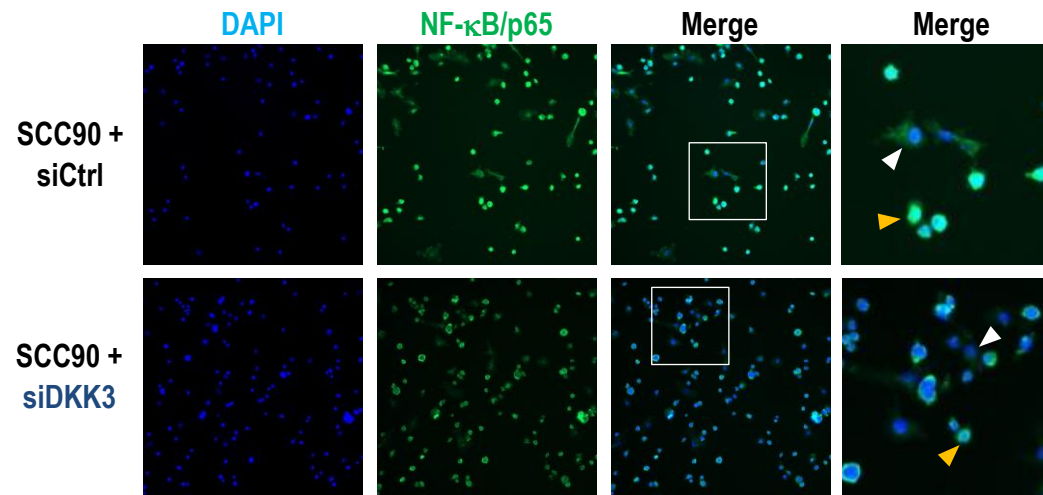
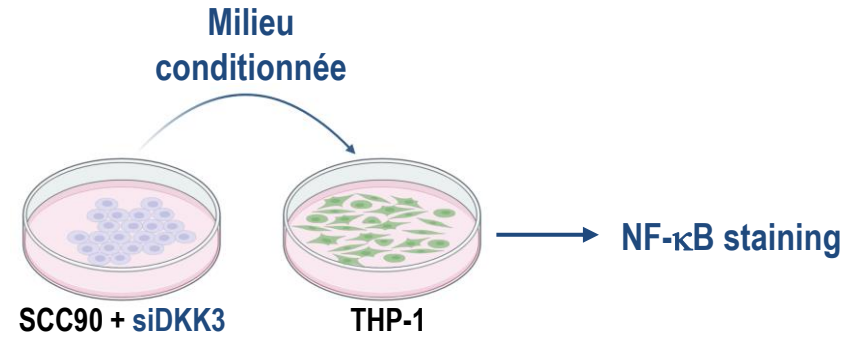
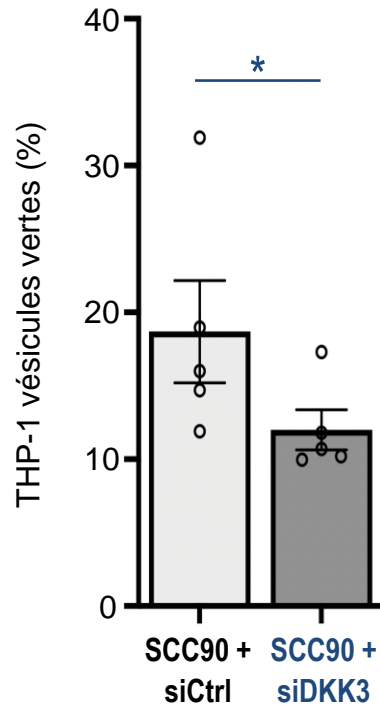
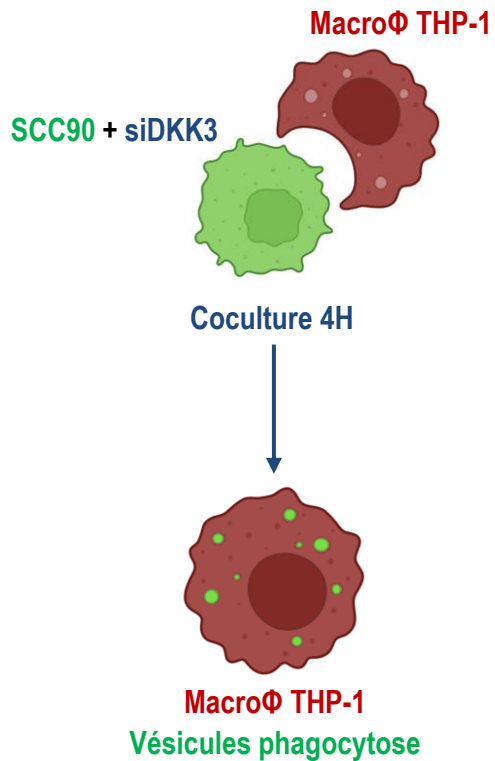
- Cytokines/Interleukins
- Immune response/Response to pathogens
- Cell migration/Locomotion
- Response to stimulus/Signaling

Top 100 downregulated genes

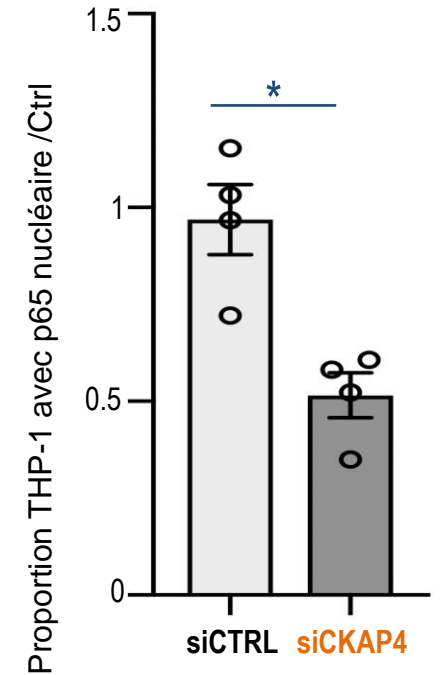
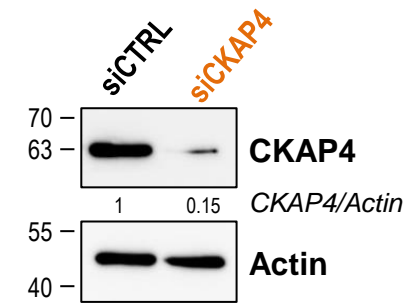
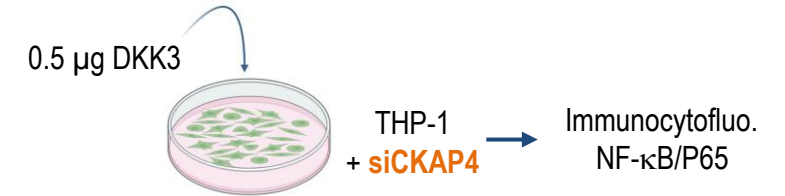
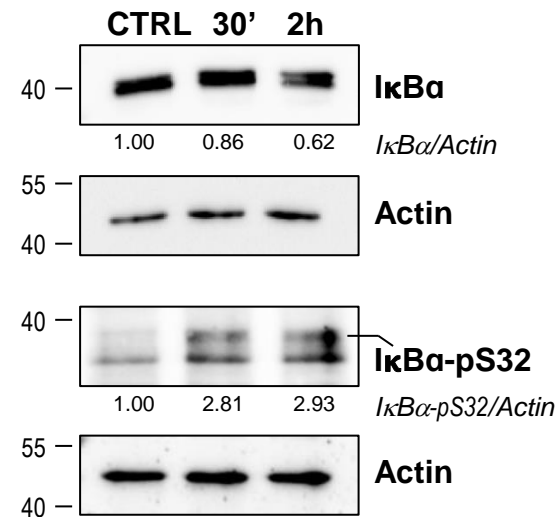
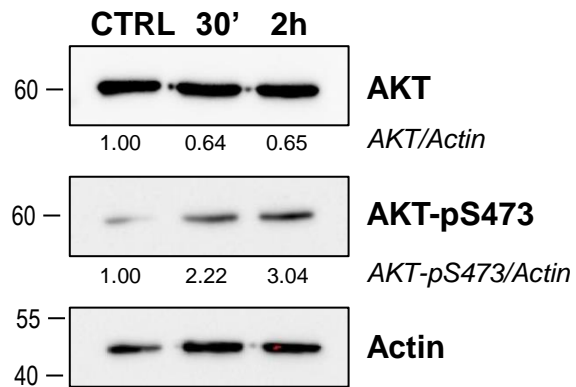
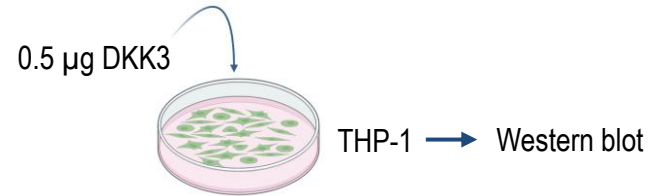
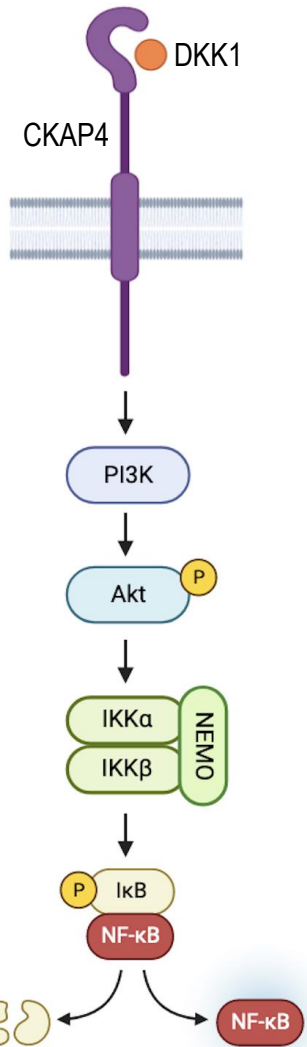


DKK3 STIMULE LA VOIE NF-KB ET LA PHAGOCYTOSE DE CELLULES CANCÉREUSES

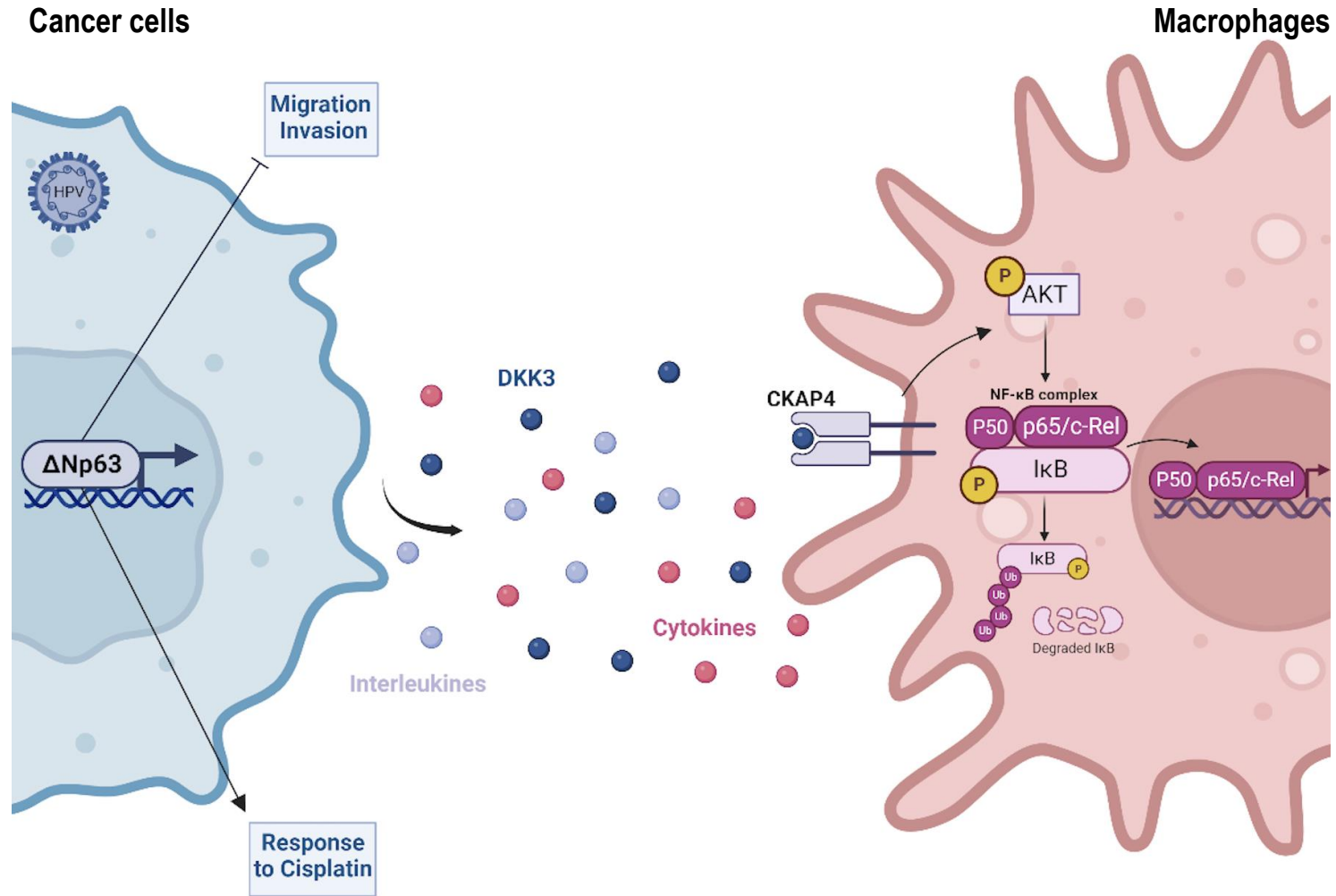
In vitro phagocytosis assay



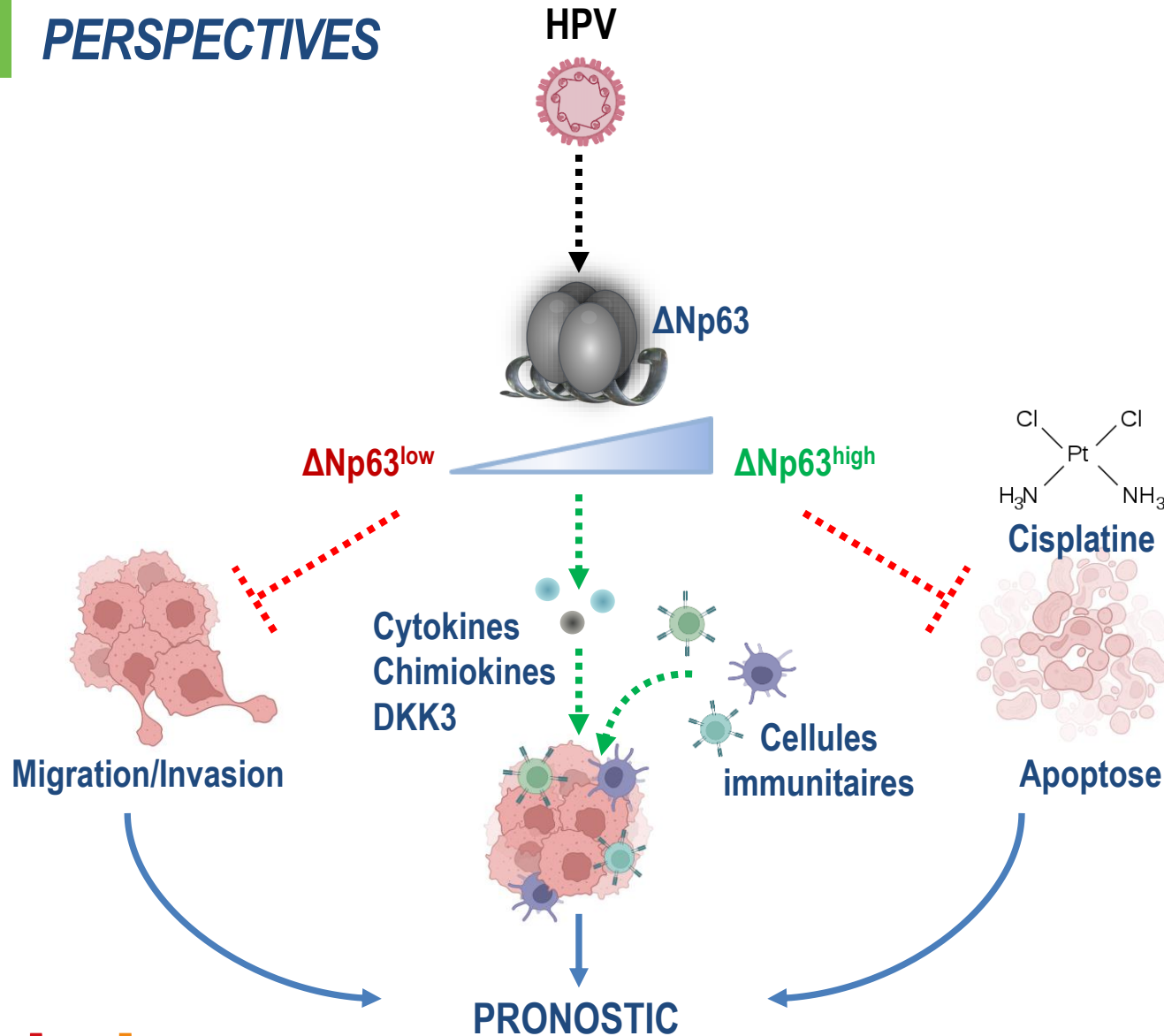
DKK3 STIMULE LA VOIE NF-KB ET LA PHAGOCYTOSE DE CELLULES CANCÉREUSES



CONCLUSIONS



PERSPECTIVES



- **Origines** du **gradient d'expression** de $\Delta Np63$ dans les tumeurs oropharyngées HPV-positives?
- **Programme transcriptionnel** pouvant être valorisé à travers l'identification de **marqueurs pronostiques**?
- **Impact** de $\Delta Np63$ sur l'**immunogénéicité** des cellules tumorales? **Sécrétome/protéines membranaires**?
- **Conséquences** précises pour le **microenvironnement**?
- Intérêt pour la **stratification des patients**?

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Justine DE AZEVEDO – Doctorante

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