



HAL
open science

UMR 9018 - Team 2 - “ Host-tumor interactions in Head and Neck Carcinomas ”

Pierre Busson, Karim Benihoud, Thierry Ragot, Léna Zig, Ai Aurore Gelin, Tcs Tram, Thi Bao Tran, Salomé Laurans, François Moreau, Sarah Awan Toor

► To cite this version:

Pierre Busson, Karim Benihoud, Thierry Ragot, Léna Zig, Ai Aurore Gelin, et al.. UMR 9018 - Team 2 - “ Host-tumor interactions in Head and Neck Carcinomas ”. Visite du directeur du CNRS Antoine Petit à l'UMR 9018-METSY à Gustave Roussy, Dec 2020, Villejuif, France. hal-03087131

HAL Id: hal-03087131

<https://hal.science/hal-03087131>

Submitted on 23 Dec 2020

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

UMR 9018- Team 2

« Host-tumor interactions in Head and Neck Carcinomas » (Pierre Busson / Karim Benihoud)

Composition de l'équipe

- Pierre Busson, DR1 responsable de l'équipe
- Karim Benihoud, PR1 Paris Saclay, co-responsable de l'équipe
- Thierry Ragot, CRCN
- Léna Zig, AI
- Aurore Gelin, TCS
- Tram Thi Bao Tran, doctorante
- Salomé Laurans, doctorante
- François Moreau, IE
- Sarah Awan Toor, IE



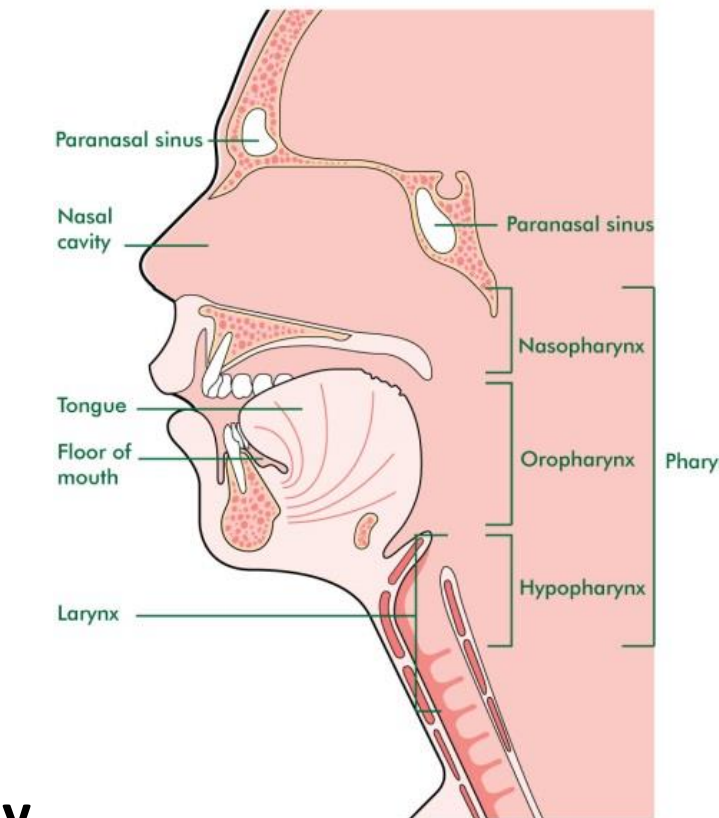
Cliniciens rattachés à l'équipe

- Ingrid Breuskin, chirurgie ORL
- Philippe Gorphe, chirurgie ORL
- Caroline Even, oncologie médicale

Main characteristics of Head and Neck carcinomas (HNCs)

General background

- Public health problem
- Exposure to carcinogens (tobacco, alcohol, ...)
- Possible etiologic contributions of viruses e.g. Human PapillomaVirus
- Systemic diseases :
 - Multiple factors of immune escape
 - Cachexia and muscle wasting



Institutional context

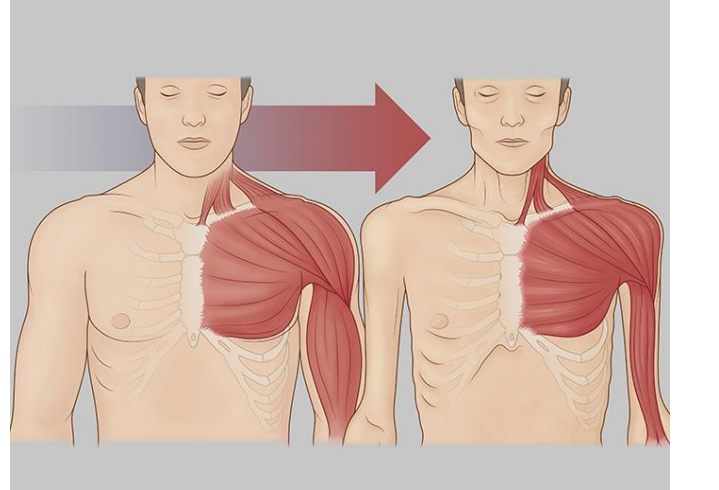
- Excellent medical performances at Gustave Roussy
- Previous collaborations on nasopharyngeal carcinomas
- A need for broader projects in basic and translational research

Immunological and metabolic aspects of HNCs

Immunological aspects:

- Objective responses to anti-PD1/PD-L1 in 15%-20% cases
- 50% of patients non-eligible because of cachexia
- Mechanisms of primary and secondary resistances under investigation

High prevalence of cachexia



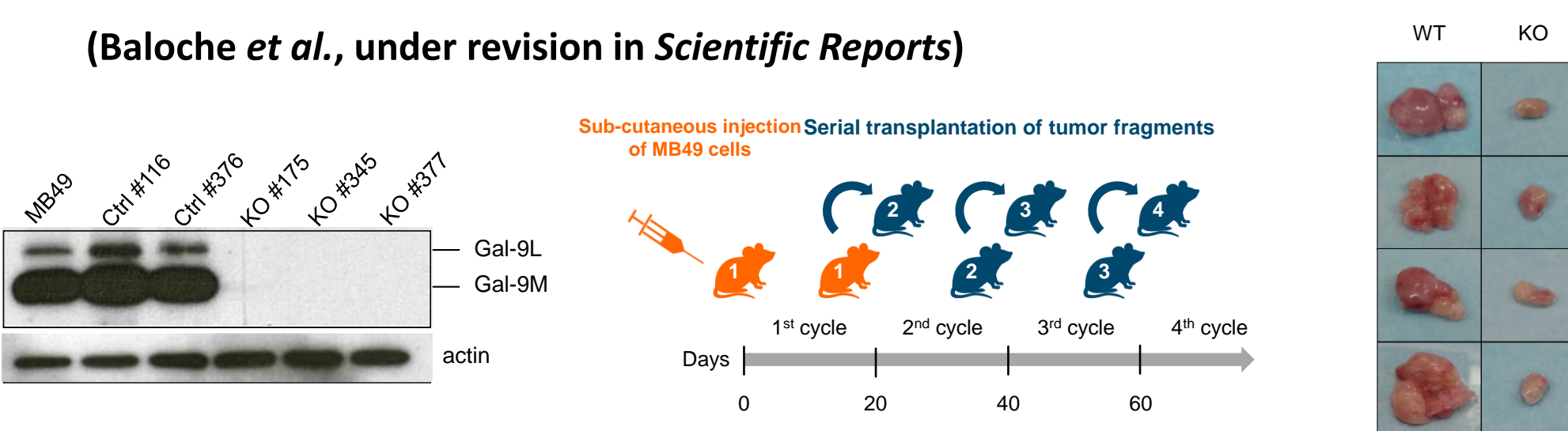
Two approaches against tumor immune suppression:

- Neutralisation of suppressive factors in the tumor microenvironment (focus on extra-cellular galectin-9)
- Stimulation of the immune response against tumor antigens (vaccination using recombinant adenoviruses)

Extra-cellular galectin-9 and HNCs

Recent achievements

- Obtention and characterization of murine tumor models KO for Gal-9 (Baloche *et al.*, under revision in *Scientific Reports*)

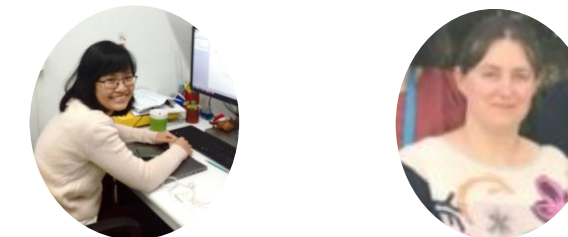


- Patent on antibodies neutralizing extra-cellular galectin-9 licensed to HifiBio Therapeutics since February 2017

WO 2015/185875 A2

Galectin-9 and HNCs: ongoing projects

- Characterization of human T-lymphocytes resistant to apoptosis induced by gal-9
- Investigations on plasma gal-9 in HNC patients with primary or secondary resistances to anti-PD1/PD-L1



Staff: P. Busson, A. Gelin, T. Thi Bao Tram

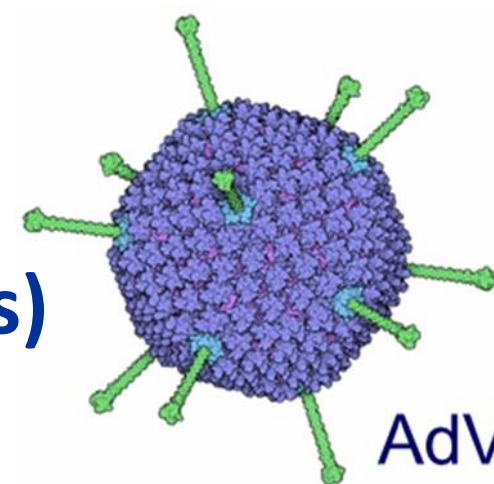
Funding: HifiBio Therapeutics, current application to Unicancer

Galectin-9 and HNCs: collaborations

- Jiang Li, Sun Yat-Sen University Cancer Center, Canton
- Udo Kontny, Uniklinik RWTH, université d'Aix la Chapelle
- Olivier Dellis, Inserm UMR 1174, université Paris-Saclay
- Nao Yamagawa, plateforme PAGés, UMR 8576, univ. de Lille
- Nadira Delhem and Olivier Morales, Inst. de Biologie de Lille

Adenoviral vaccinations

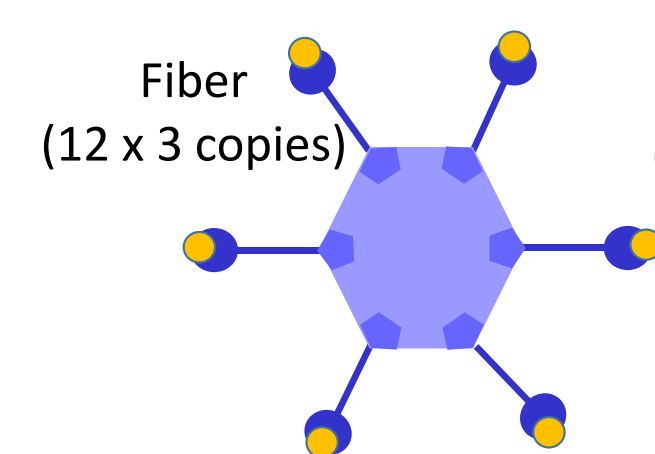
Recent achievements (ongoing publications)



- Successful mouse immunisation against HPV L2 or E6/E7 using epitope display on adenovirus capsid (Ramdani *et al.* in preparation)
- Induction of humoral and cellular responses against a model antigen using protein display on bacteriophage T5 capsid (Ramdani *et al.* in preparation, patent deposit PCT/FR2020/051628)

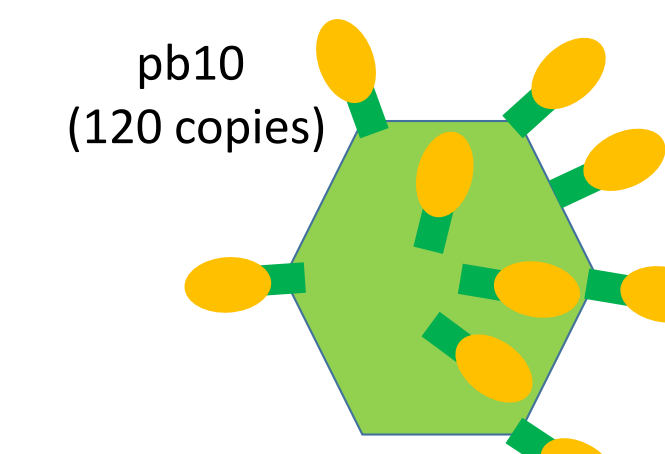
Vaccination platforms

Adenoviral platform
WO 2012/150478



Epitope display

Phage T5 platform
PCT/FR2020/051628
Collaboration P. Boulanger



Protein display

Adenovirus: collaborations

- Pierre Bobé, équipe Immunorégulation, Chimokines et Persistance Virale, INSERM UMR 996, Clamart
- Pascale Boulanger, équipe Bactériophage T5, Institut de biologie intégrative de la cellule (I2BC), CNRS UMR, Orsay
- Sophie Dupré, laboratoire chimie physique, CNRS UMR 8000, Orsay
- Anja Ehrhardt, Witten university, Witten, Germany
- Pascal Fender, équipe Adénovirus, Institut de biologie structurale, Grenoble

Adenoviral vaccinations: ongoing projects

- Development of adenovirus vectors and oncolytic adenoviruses targeting HNCs
- Characterization of adenovirus interaction with blood components
- *In situ* vaccination with oncolytic adenoviruses

Staff: K. Benihoud, L. Zig, F. Moreau, S. Laurans

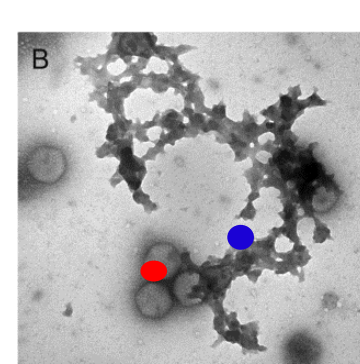
Funding: ANR

Other projects

Combination of adenoviral transduction and electro-permeabilisation

« Metallic particles generated during millisecond pulse application enhance adenovirus-mediated gene transfer in CAR-negative cells »

Close to submission



Viral particles
Metal particles



Thierry Ragot
CRCN CNRS

Novel therapeutic approaches for EBV associated malignancies

- Collaboration with T. Messick (Wistar Institute and Cullinan Oncology)
- NCT03682055 - VK 2019 anti-EBNA1 small molecules on trial in various centers including Gustave Roussy (Caroline Even, Clémentine Sarkozy, Jean-Marie Michot)
- Collaboration with Viracta Therapeutics on a compound inducing EBV lytic cycle in NPC cells



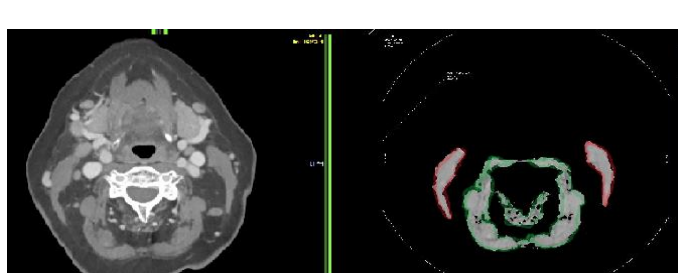
Caroline Even,
oncologue médicale

➢ Manuscript in preparation



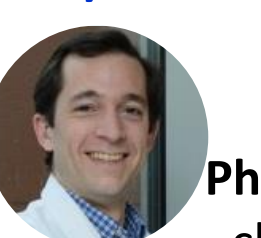
Functional genomics of cachexia and sarcopenia in HNCs

General aim : to take advantage of reconstructive surgery for exploration of muscle alterations *in situ*



Pilot study performed by H. Hachicha (DUERTECC – 2018/2019)

Abstract submitted to AACR 2021 : « Cellular and molecular alterations of sarcopenic muscles in Head and Neck carcinomas »



Philippe Gorphe,
chirurgien ORL

Ancillary study of Magnolia (ongoing PHRC)



Collection of muscle fragments

- ➔ RNA-seq
- ➔ Metabolic profile
- ➔ Epigenetic profile

- Correlations with clinical observations and outcome ?
- Confirmation of c-IAP2 overexpression ?