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

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HAL Authorization

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

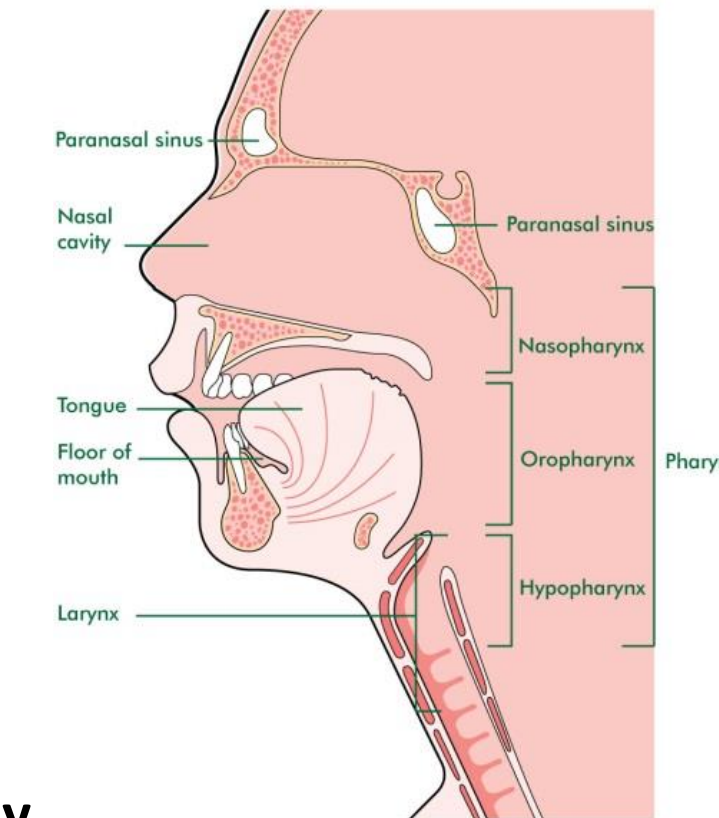
- Ingrid Breuskin, chirurgie ORL
- Philippe Gorphe, chirurgie ORL
- Caroline Even, oncologie médicale



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

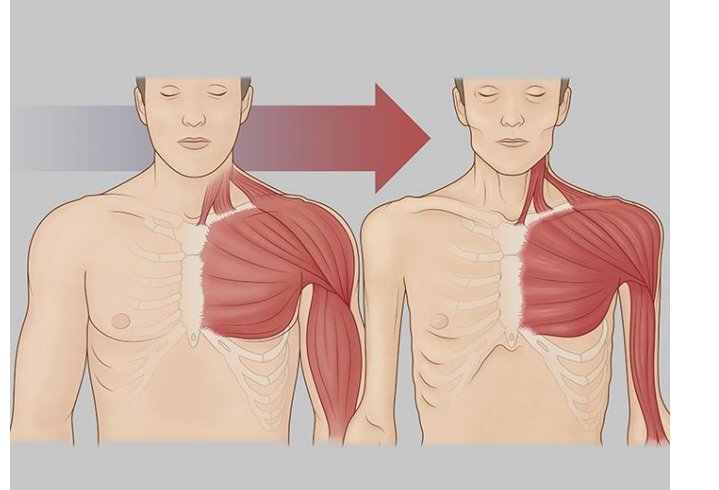
- Excellent medical performances at Gustave Roussy
- Previous collaborations on nasopharyngeal carcinomas
- A need for broader projects in basic and translational research

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



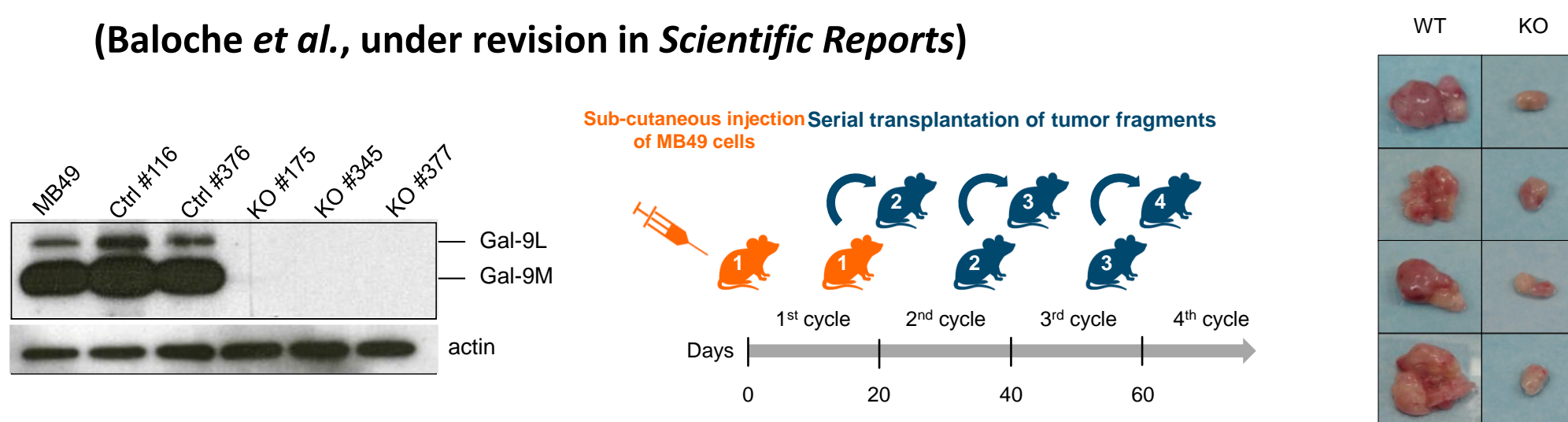
Two approaches against tumor immune suppression:

- 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

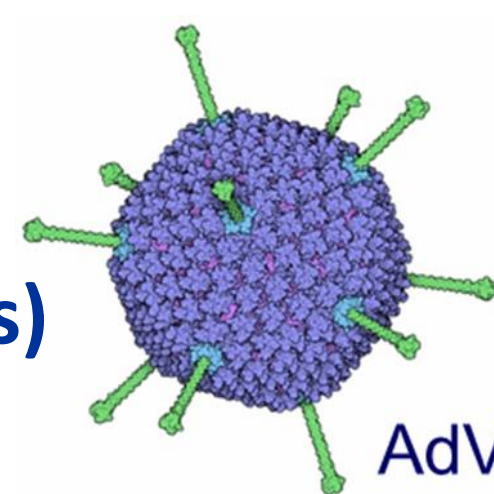
Funding: HifiBio Therapeutics, current application to Unicancer

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

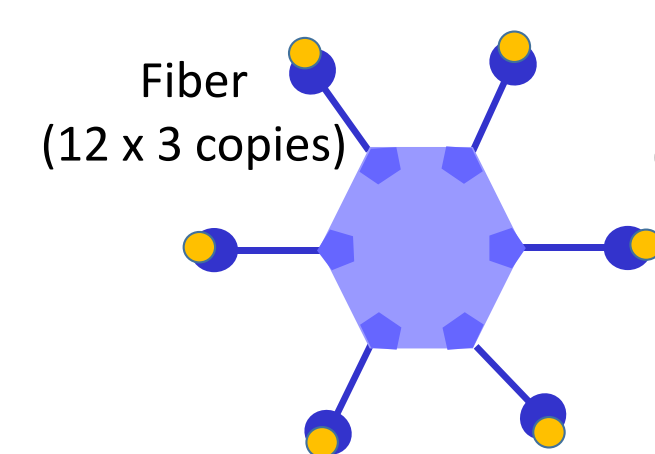
Recent achievements (ongoing publications)



- 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)

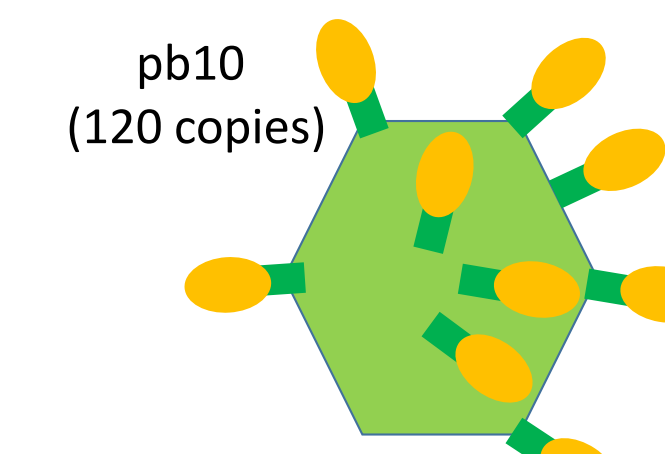
Vaccination platforms

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

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
- Manuscript in preparation

Structure-based design of small molecule inhibitors of EBNA1 DNA binding blocks Epstein-Barr virus latent infection and tumor growth

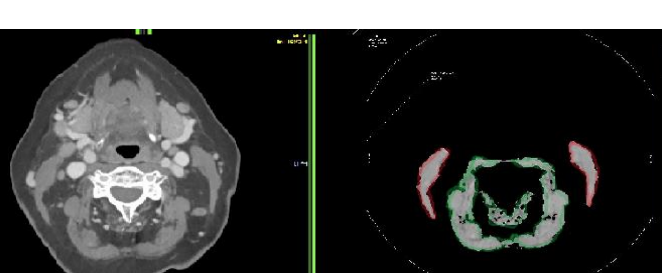


Caroline Even, oncologue médicale



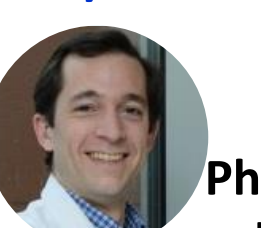
Functional genomics of cachexia and sarcopenia in HNCs

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



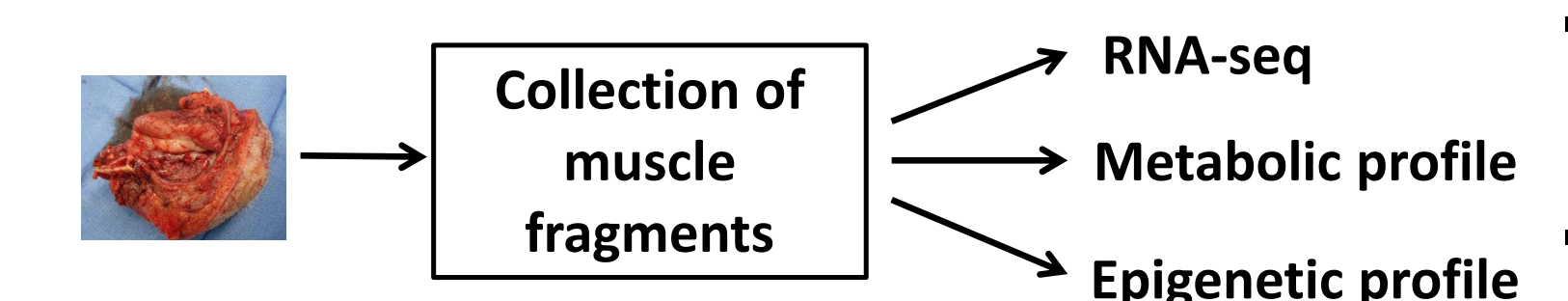
Pilot study performed by H. Hachicha (DUERTECC – 2018/2019)

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)



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

Other projects

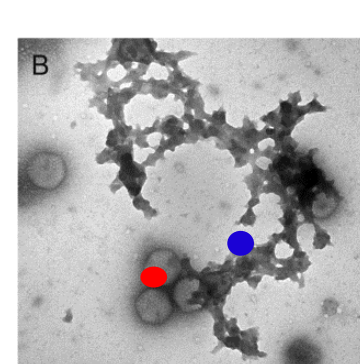
Combination of adenoviral transduction and electro-permeabilisation

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

Close to submission



Thierry Ragot, CRCN CNRS



Viral particles
Metal particles