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VRIJE UNIVERSITEIT BRUSSEL

PhD in Medical Sciences
2021-2022

INVITATION to the Public defence of

## Philippe GIRON

To obtain the academic degree of

**'DOCTOR OF MEDICAL SCIENCES'**

# EXPLOITING GENOMIC VULNERABILITIES IN LUNG CANCER FOR THERAPEUTIC TARGETING

The public defence will take place on

**Tuesday**, **3 May 2022 at 5 p.m.**

**In Auditorium Vanden Driessche**
Faculty of Medicine and Pharmacy, Laarbeeklaan 103, 1090 Brussel

Please contact the PhD candidate if you want to attend the public defence.

## Summary of the dissertation

Non-small cell lung cancer (NSCLC) is a disease with high incidence and is associated with high disease related mortality. First, we describe that targeting USP13 in EGFR mutant NSCLC decreases the protein stability of EGFR and increases the sensitivity to EGFR inhibition with small molecules in vitro and in vivo. Second, we identified that for the treatment of non-V600 BRAF mutant NSCLC, type II RAF inhibitors have greater therapeutic effect (in vitro) compared to type I RAF inhibitors, both as a single agent and combined with trametinib. Lastly, we characterized two novel CRAF mutations found in a NSCLC cohort and identified that CRAF P261A mutation can provide oncogenic properties to cells, and that such cells are sensitive to combined MEK and type II RAF inhibitors. In conclusion, this PhD work contributes to the understanding and targeting of functional insensitivity to existing EGFR targeted therapies, further established safe and effective actionability of non-V600 BRAF mutations and identified a novel targetable driver CRAF in NSCLC which is also actionable.

## Curriculum Vitae

Philippe Giron is currently active as a scientific collaborator at the centre of genetics, where he is responsible for the genetic analysis and interpretation of somatic mutations in tumour samples and the germline testing of colon cancer predisposition. From this position, Philippe is continuing the research of atypical RAF mutations and other variants with unknown significance. During his PhD he was active in several (lung) cancer related research projects, resulting to 14 published works, of which 3 first-author research papers. The main projects focussed on (1) the improvement of existing EGFR targeted therapies in NSCLC, (2) improvement of non-V600 BRAF mutants in NSCLC, and (3) the characterisation and targeting of novel CRAF mutations found in NSCLC. During his Master project, Philippe worked on the development of non-viral ultrasound triggered dendritic cell immunotherapy. Through these projects, Philippe specialized in molecular genetics and translational molecular oncology.