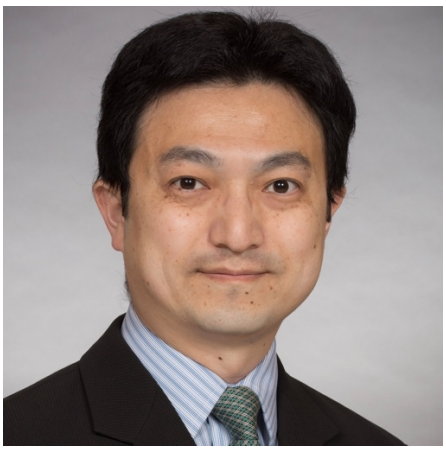

10th of September 2025

Building K3, Room 4.1 (4th floor)
University Hospital Ghent

Start at 14.00

Host: Prof. Dr. Dmitri Krysko
Cell Death Investigation and Therapy Laboratory

The title of the seminar:

"Caffeine and Epigenetics: Novel Approaches to Prevent and Treat UV-Induced Skin Cancer"

Masaoki Kawasumi, MD, PhD
Associate Professor of Dermatology
Department of Dermatology, The Ohio State University, Columbus, Ohio, USA
Secretary, American Society for Photobiology (ASP)

Skin cancer is the most prevalent cancer in the United States and is strongly associated with ultraviolet (UV) radiation that damages DNA and generates many mutations. It is critical to avoid excessive sunlight in order to prevent skin cancer. Also, chemoprevention is of great interest. Human epidemiological studies and our mouse studies showed that caffeine prevents UV-induced skin carcinogenesis. We found that the most relevant target of caffeine for skin cancer prevention is the ATR kinase, which senses UV-induced DNA lesions and stops the cell cycle. Genetic inhibition of ATR augmented UV-induced apoptosis and suppressed UV-induced skin cancer development.

UV-induced skin cancer has not only genetic mutations but also epigenetic abnormalities which may affect gene expression levels. Our mouse study showed that topical application of caffeine to mouse back skin reduced the frequency of *Cdkn2a/p16* promoter mutations. These mutations inhibited the binding of ETS transcription factors, likely reducing the expression of the p16 tumor suppressor. Furthermore, our sequencing analyses of skin cancer identified the gene whose expression is downregulated and whose promoter is methylated, potentially contributing to aggressiveness of skin cancer.

We have been developing CRISPR-Cas9-based epigenome editing tools to change DNA/histone modifications specifically at a genomic region of interest. We targeted the p16 promoter that is methylated in skin cancer, thereby silencing p16. By using our epigenome editing tools, we were able to reactivate p16 and inhibit cell proliferation. These epigenome editing tools have many possibilities to regulate the expression of cancer-related genes in order to inhibit cancer phenotypes.