Board of examiners

**Prof. Dr. Eric Deutsch**
Department of Radiation Oncology
South-Paris University

**Prof. Dr. Carine Michiels**
Laboratory of Cellular Biochemistry and Biology
University of Namur

**Prof. Dr. Nico Buls**
Department of Radiology
Vrije Universiteit Brusse/UZ Brussel

**Dr. Inès Dufait**
Department of Radiotherapy/Medical Oncology
UZ Brussel

**Prof. Dr. Johan De Mey, Chair**
Department of Radiology
Vrije Universiteit Brussel/UZ Brussel

**Prof. Dr. Mark De Ridder, Promoter**
Department of Radiotherapy
Vrije Universiteit Brussel/UZ Brussel

**Dr. Heng Jiang, Co-promoter**
Department of Radiotherapy
UZ Brussel

VRIJE UNIVERSITEIT BRUSSEL

PhD in Medical Sciences
2019-2020

INVITATION to the Public defence of

**Hui WANG**

To obtain the academic degree of **'DOCTOR OF MEDICAL SCIENCES'**

# Improve radioresponse by targeting redox homeostasis: defeat the enemy by breaking the balance.

**Thursday, 6 February 2020 at 5 p.m.**
In Auditorium **Piet Brouwer**
Faculty of Medicine and Pharmacy, Laarbeeklaan 103, 1090 Brussels

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## Summary of the dissertation

Radiotherapy is one of the mainstays of cancer treatment and applied in more than 50% of cancer patients. The biological effects induced by radiation are primarily ascribed to DNA damage caused directly by radiation or indirectly by radiation triggered reactive oxygen species (ROS). In normal cells, ROS as metabolic byproducts are rigidly regulated by antioxidant systems, such as thioredoxin (Trx) and glutathione (GSH) systems. However, in cancer cells, ROS are constantly generated at a high level due to the fast metabolism, and correspondingly antioxidant enzymes are dysregulated, which is correlated with poor outcome, making them potential targets to be integrated with radiation. So in the first part of this thesis, we explored the radiosensitizing effect of auranofin (AF), an anti-arthritic drug and inhibitor of Trx reductase. We demonstrated that AF counteracted radioresistance of breast cancer cells with mechanisms linked to overproduction of ROS and ROS mediated detrimental biological alterations. Moreover, when incorporated with buthionine sulfoximine, an inhibitor of GSH system, the radiosensitization was amplified in both in vitro and vivo models. In the second part, by exploring natural compound piperlongumine (PL), an inhibitor of both GSH and TrxR systems, we revealed that PL enhanced radiosensitivity in both colorectal and breast cancer cells. In addition, PL improved the tumor response to both single and fractionated radiation via increased oxidative stress. To conclude, targeting antioxidant systems is an appealing strategy to enhance radiation response, and AF and PL have great promise to be developed as radiosensitizers.

## Curriculum Vitae

Hui Wang obtained her Master degree in East China Normal University in 2012. She joined the Department of Translational Radiation Oncology, Physics and Supportive Care (TROP) in 2014 as a PhD candidate under the supervision of Prof. dr. Mark De Ridder and Dr. Heng Jiang. Her PhD project aimed to investigate the radiosensitizing properties of antioxidant system inhibitors auranofin and piperlongumine.

During her PhD, Hui has published 2 research papers as first author and 2 review articles. She presented her research at multiple international and national conferences. In 2017, She was awarded Evds scholarship from Kom op Tegen Kanker.