

Report for the French Embassy sponsored workshop on

“The extended Hippo tumour suppressor pathway in cancer cell signalling and autophagy”

Report prepared by Dr. Alexander Hergovich, UCL Cancer Institute

Executive Summary

The workshop “The extended Hippo tumour suppressor pathway in cancer cell signalling and autophagy”, funded by the French Embassy, was held on 27th and 28th August 2015 in meeting room G31 of the Rockefeller building, University College London. The original goals of the works were to:

- Bring together internationally recognised scientists from UCL and France with central interests in extended Hippo signalling and autophagy.
- Strengthen already existing collaborations between UCL and French research laboratories.
- Establish novel collaborative approaches between different disciplinary and methodological research backgrounds.
- Establish strategies for collaborative funding applications to major funding agencies such as the ERC.

The workshop was attended by six academics and researchers from France, specifically coming from the Institut Curie (Paris), the University Paris Decartes-Sorbonne (Paris), the Institut Necker Enfants-Malades (Paris), University Caen-Basse Normandie (Caen), and the Cancer Research Center of Toulouse. These French scientists were joined by five academics from the UCL Cancer Institute and the MRC LMCB (UCL). Unfortunately, Prof. Paolo Salomoni from the UCL Cancer Institute and Prof. Mario Pende from the Institut Necker Enfants-Malades (Paris) could not attend the workshop. All participants shared yet unpublished work, enjoyed the collaborative environment and rated the workshop as very successful. Overall, the original objectives were successfully achieved with a substantial number of initiatives being planned for future collaborations. Joint publications have already been published or submitted to peer-reviewed journals, and discussions regarding a follow up workshop to be held in France have been initiated.



Photo of the workshop participants in the meeting room of the Rockefeller building (UCL).
Note: Prof. Paolo Salomoni is not in the picture.

Workshop programme

Thursday (August 27th 2015)

- 11:45-13:00 Arrival of French participants (lunch sandwiches and refreshments)
- 13:00-13:15 Welcome of all participants
- 13:15-15:00 **Workshop part 1 – The Hippo pathway in cancer cell signalling**
- 13:15-13:40 *The Hippo pathway: a complex signalling network*
Dr. Alex Hergovich (Cancer Institute, UCL)
 - 13:40-14:20 *Connecting RASSF1A/migration/metastasis with a quick insight into mechanistic: RASSF1A/YAP/RhoB/GEFH1 & PP2A*
Prof. Gerard Zalcman (University Caen-Basse Normandie, Caen)
 - 14:20-15:00 *Merlin/NF2 interacts with nuclear tumor suppressor proteins involved in transcription elongation*
Dr. Pablo Rodriguez-Viciano (Cancer Institute, UCL)
- 15:00-15:30 Tea/coffee Break
- 15:30-17:30 **Workshop part 2 – The Hippo pathway and autophagy**
- 15:30-16:10 *The STK38 kinase is a new Beclin1 partner positively regulating autophagy*
Dr. Carine Joffre (Cancer Research Center of Toulouse, Toulouse)
 - 16:10-16:50 *RAS-driven oncogenic transformation is promoted by NDR1-mediated macroautophagy and mitophagy*
Prof. Jacques Camonis (Institut Curie, Paris)
 - 16:50-17:30 *Regulation of YAP by mTOR and autophagy: a therapeutic target of tuberous sclerosis complex*
Dr. Ning Liang / Prof. Mario Pende (Institut Necker Enfants-Malades, Paris)
- 17:30-18:00 Tea/coffee Break
- 18:00-18:40 **Workshop part 3 – Focus on autophagy (part 1)**
- 18:00-18:40 *Role of plasma membrane-endoplasmic reticulum contact sites in autophagosome biogenesis*
Prof. Patrice Codogno (University Paris Decartes-Sorbonne, Paris)
- 19:15-22:00 Dinner at Tas Restaurant (Gower Street)

Friday (August 28th 2015)

- 09:00-09:15 Arrival of participants
- 09:15-10:35 **Workshop 4 – Focus on autophagy (part 2)**
- 09:15-09:55 *Discovering new autophagy modulators as novel anti-cancer targets*
Dr. Ivana Bjedov (Cancer Institute, UCL)
 - 09:55-10:35 *The regulation of ATG4B as a potential pathway for drug targeting*
Dr. Robin Ketteler (MRC LMB, UCL)
- 10:35-11:00 Tea/coffee Break
- 11:00-11:00 **Workshop 4 – The Hippo pathway and autophagy (collaborative potential)**
- 11:00-11:05 Brief overview of proposals with collaborative potential
Dr. Alex Hergovich (UCL Cancer Institute)
 - 11:05-11:35 Short presentations of specific ideas followed by open discussion
 - 11:05-11:15 *Mechanistic linking RASSF1A/YAP and RhoB*
Prof. Gerard Zalcman (University Caen-Basse Normandie, Caen)
 - 11:15-11:25 *Autophagy, primary cilium and Hippo pathway*
Prof. Patrice Codogno (Institut Necker Enfants-Malades, Paris)
 - 11:25-11:35 *Understanding autophagosome-lysosome fusion using CRISPR screening*
Dr. Robin Ketteler (MRC LMB, UCL)
- 11:35-12:30 Round table discussion
- 12:30-14:00 Lunch (cont'd discussion)
- 14:00 Departure of participants

Participant List (in alphabetical order)

Dr. Ivana Bjedov, Senior research fellow at the UCL Cancer Institute.
Expert in autophagy- and ageing-related signalling.

Prof. Jacques Camonis, Research director at the Institut Curie in Paris.
Expert in GTPase-mediated cancer cell signalling.

Prof. Patrice Codogno, Research director at the University Paris-Decartes Sorbonne.
Expert in autophagy and autophagy-related signalling processes.

Dr. Alexander Hergovich, Senior research fellow at the UCL Cancer Institute.
Expert in Hippo kinase signalling.

Dr. Carine Joffre, Post-doctoral researcher at the Cancer Research Center Toulouse.
Expert in cancer and autophagy signalling.

Dr. Robin Ketteler, Senior research fellow at the MRC LMCB institute (UCL).
Expert in autophagy signalling and large scale screening approaches.

Dr. Guenaelle Levallet, Senior researcher at the University Baen-Basse Normandie.
Expert in molecular and cellular research of lung cancer signalling.

Dr. Ning Liang, Post-doctoral researcher at the Institute Necker Enfants-Malades in Paris.
Expert in Hippo and autophagy signalling.

Dr. Pablo Rodriguez-Viciiana, Senior lecturer at the UCL Cancer Institute.
Expert in oncogenic and tumour suppressive cell signalling.

Prof. Gerard Zalcman, Research director and clinician at the University Baen-Basse Normandie.
Expert in basic and clinical research of human lung cancer signalling.

Initiatives for Future Collaborations

Research projects identified to take forward:

- Prof. Zalcman and Dr. Hergovich will study the role(s) of the NDR1/2 protein kinases in lung cancer cells with loss-of-function of the RASSF1A tumour suppressor protein.
- Dr. Rodriguez-Viciana supported by different participants of this workshop will pursue the roles of Hippo signalling in the regulation of transcription elongation.
- Prof. Camonis, Prof. Codogno and Dr. Hergovich will study novel and unexpected aspects of Hippo kinases in the regulation of specific autophagic events.
- Dr. Bjedov could secure the support of Prof. Codogno regarding her studies of autophagy-regulating components in the context of healthy ageing.
- Dr. Ketteler will start to pursue different autophagy- or methodology-related aspects in collaboration with Dr. Joffre and Dr. Hergovich.
- In general, many participants expressed great interest in collaborating with Dr. Ketteler as head of the screening facilities at the MRC LMCB at UCL.

Collaborations leading to journal publications:

The following collaborative manuscripts have already been published or are currently under revision in internationally recognised peer-reviewed journals:

- Bettoun, A., Joffre, C., Parrini, M.C., Gundogdu, R., Sharif, A.A.D., Gomez, M., Cascone, I., Meunier, B., Zago, G., Surdez, D., Vallerand, D., White, M.A., Codogno, P., Camonis, J., and Hergovich, A. *NDR1-mediated mitophagy supports Ras-driven oncogenic transformation. Autophagy* (2015AUTO0661) manuscript under review
- Dubois, F., Keller, M., Calvayrac, O., Soncin, F., Hoa, L., Hergovich, A., Parrini, M.C., Vaisse-Lesteven, M., Camonis, J., Levallet, G., and Zalcman, G. *RASSF1A is a tumor and invasion-suppressor, regulating YAP and GEF-H1/RhoB signaling in human Non-Small Cell Lung Cancer. Cancer Research* (CAN-15-1008) revised manuscript re-submitted
- Joffre, C., Dupont, N., Hoa, L., Gomez, V., Pardo, R., Goncalves-Pimentel, C., Achard, P., Bettoun, A., Meunier, B., Bauvy, C., Cascone, I., Codogno, P., Fanto, M., Hergovich, A., and Camonis, J. *The pro-apoptotic STK38 kinase is a new Beclin1 partner positively regulating autophagy. Current Biology* 25(19): 2479-2492 (2015).

Follow-up workshops:

The participants have agreed that this initial French Embassy sponsored workshop should be considered as a starting point for follow-up workshops. Hopefully, the participants will be able to secure the required funding for a follow-up workshop to be held in France in 2016.

Funding opportunities to be explored for further exchanges / seed funding for projects:

UCL Impact and other co-funded studentships

<https://www.ucl.ac.uk/slms/enterprise/funding>

<https://www.ucl.ac.uk/enterprise/sponsored-studentships/co-funded-studentships>

UCL Graduate School research project funding

<http://www.grad.ucl.ac.uk/funds/>

French National Research Agency funding

<http://www.agence-nationale-recherche.fr/en/project-based-funding-to-advance-french-research/>

Horizon 2020 funding from the European Union

<https://ec.europa.eu/research/participants/portal/desktop/en/home.html>

Finance

The provided funding has been spent to cover the travel (train or air travel from France to London and return) and accommodation (one night accommodation in central London) of the French participants. The generous funds provided by the French Embassy also covered the lunches, refreshments and workshop dinner during the duration of the workshop.

Final Remarks

The author of this report as well as all participants of the workshop would like to genuinely thank the French Embassy for providing the funds required to run this workshop. Although some collaborative interactions already existed between some participating UCL and French laboratories prior to this workshop, this workshop has sparked novel synergies between the participating institutions and laboratories. As outlined above new and exciting research avenues and initiatives have been fostered, enabling the development of strong, stable and lasting collaborations between UCL and France.

Considering the confidential nature of some of the content of this report (e.g. newly identified research projects), we hope that this report will not be distributed publically (e.g. posted online).