

Report on Dr Agnieszka Wolnicka-Glubisz' scientific career:
presentation to be recognized as habilitated to direct scientific research.

Dr Agnieszka Wolnick-Glubisz has started her scientific career as an independent researcher after she has defended her PhD thesis in 2002, on the work achieved in the Biophysics Department of the Faculty of Biotechnology of the Jagiellonian University in Krakow, Poland.

Dr Agnieszka Wolnicka-Glubisz has taken a research direction by herself decided in order to achieve a post doctoral stay in the USA for three years. The laboratory "Photobiology and photoimmunology" of the George Washington University Medical center in Washington DC was the proper place where the candidate could specialize in addressing the biological aspect of the melanin induced key reactions in cell. Their consequences for the skin reaction and organism response to the ultra violet radiation which are the main inducers of melanin and the subsequent pathologies as cancer and precisely melanoma are of fundamental importance.

In this context, Dr Agnieszka Wolnicka-Glubisz describes her scientific achievement for habilitation as entitled:

Inflammation and melanoma as effect of UV radiation on skin in selected mouse models.

The model: HGF/SF hyper expressing FVB mice, is extremely favorable and precious to study the close-to-human process of melanoma development for:

- ✓ Dermal propagation
- ✓ UV sensitivity
- ✓ Inflammation dependency
- ✓ Reproducibility



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During the progress of Dr Agnieszka Wolnicka-Glubisz' research this model has been adequately used to uncover several important biological features of the skin melanoma appearance and development.

A. The process of inflammation which occurs in the skin when UV rays are applied is limited to adults. The lack of inflammation reaction in neonates is related to the amount and expression of HGF/SF. Thus, as inflammation when resolved, is a reaction to cancer development, the hypothesis that lack of inflammation reaction is favoring cancerization could be raised and is possible. The overexpression of HGF in adult decreases the inflammation confirming the above hypothesis.

Dr Agnieszka Wolnicka-Glubisz here expresses the level of her participation in the work. This is not done in the other parts of work described. One can assume that she was the PI.

This description ends with a table which would be helpful if it was clear. It gives data in terms as + or ++ without expressing what + means... this is surprising from a habilitation applicant.

B. Dr Agnieszka Wolnicka-Glubisz has deciphered an important aspect of the role of melanocortin 1 receptor as compared to Mc2r or Mc3r in skin inflammation /tolerance induced upon UV radiation. In this part, no description of the level of participation.

C. Interestingly Dr Agnieszka Wolnicka-Glubisz has brought an expertise of which she could take advantage for her new research activities back to Poland and to the Jagiellonian University. She has demonstrated, considering the possible incidence of the quality of melanin on the cancerization process in melanoma, that HGF/SF does not affect either quality or efficacy of melanin production.

D. Dr Agnieszka Wolnicka-Glubisz has finally insisted in this report on her demonstration, in a recently published paper in Intl J. Cancer, of the role of Mc1r in UV induced melanoma in HGF hyper expressing mice. Here, HGF is overexpressed in C57BL/6 mice and the work shows very nicely the difference of sensitivity to UV for the development of melanoma according to the Mc1r action in pigmentation and the link between Mc1R and the HGF/Met signaling pathways.

In order to explain the regulation of both pathways the candidate regulatory molecule is the tumor suppressor PTEN. This is based on the publication by Cao et al. 2013, who showed that MC1R binds competitively to PTEN avoiding its destruction by WWP2 upon ubiquitinylation and proteosomal degradation.

When UV rays activate Mc1r via alpha-MSH, this allows the complex Mc1r PTEN to be formed this protects PTEN from degradation and allows the control of PI3K, Akt, mTOR thus can counteract the HGF mediated activation of c-Met (which activates PI3K) thus decreases the cancerization. One can regret that no comment is given on the status of PDK, and the other regulators of PTEN. Moreover one should make the difference on the expression of the molecule and its activity as it is known that PTEN is an allosteric phosphatase the activity of which is highly regulated by variable microenvironment conditions.

This part of the work is very important and has potential strong medical application. It is new as the Mc1r and HGF/Met signaling in melanoma was not elucidated.

Considering the habilitation part:

It shows that Dr Agnieszka Wolnicka-Glubisz has a good ability to direct her research by developing new ways of searching and new approaches. The skills are clearly linking the biophysics to the biological problem solving and are also extremely valuable for modern research.

The acquired expertise is also exploited for the benefits of the scientific community.

The level of publication that Dr Agnieszka Wolnicka-Glubisz produces, is regularly increasing and this makes the future very promising. She has also proven that her previous and current work is attractive.

The number of students (under and post graduate) that Dr Agnieszka Wolnicka-Glubisz has taken care of is quite high. She has co promoted PhD which proves that she can be considered as deserving the habilitation.

Dr Agnieszka Wolnicka-Glubisz, is also lecturing and clearly leads the works of young students and scientists.

She develops collaborations with colleagues in the Jagiellonian university and pursues collaborations at the international level.

The work not described in the habilitation is also quite nicely related to the topic and shows a homogeneous and logical way of making the work progress as well as the intellectual progression.

This reviewer regrets thought that the English version was not carefully corrected because some sentences are not understandable. The preterit is not properly used nor spelled in many places (for example).

As far as science is concerned the habilitation is quite satisfactory I regret that there is nothing which could be called a project. This may be due to the applying rules?

Altogether : the present reviewer, considering the scientific achievement by Dr Agnieszka Wolnicka-Glubisz, her independent way of thinking and leading a research subject, ability to lead young resarchers'work and ability to communicate and teach people, wishes to express the clear support to Dr Agnieszka Wolnicka-Glubisz's habilitation.

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