Příloha 7: Posudek oponenta habilitační práce

Masarykova univerzita	
Fakulta	Lékařská fakulta MU
Habilitační obor	Lékařská biologie
Uchazeč	Yuh-Man Wadeley, Ph.D.
Pracoviště	Biologický ústav Lékařské fakulty MU
Habilitační práce	A quest to find out how human brain cells form and brain-related diseases develop
Oponent	Doc. MUDr. Milena Králíčková, Ph.D.
Pracoviště	Ústav histologie a embryologie, Lékařská fakulta v Plzni, Univerzita Karlova v Praze

Text posudku (rozsah dle zvážení oponenta)

The work contains 9 pages of introduction (text and schemes) with around 60 papers citated after this introduction. Four articles from years 2005, 2008, 2010 and 2013 are attached.

Articles from 2005 and 2008 are dedicated to the RE1 Silencing Transcription Factor (REST) which is the master regulator of neuronal and glial fate specification. It acts at multiple levels of stem cell differentiation and it is required for neurogenesis. Generations of nestin-positive, followed by β-III-tubulin-positive as well as MAP2-positive phenotype are impeded by REST ablation, and REST-depleted neural stem cells are defective in adherence, migration and survival. Findings of dr. Sun from both articles shed new light on a previously underemphasized aspect of REST function during neural differentiation.

In the third attached paper the authors including dr. Sun identified a novel neural initiator, neuronatin (Nnat) that acts as an intrinsic factor to promote neural fate in mammals as well as Xenopus. ESCs lacking this intrinsic factor fail to undergo neural induction despite the inhibition of the BMP pathway. It has recently been described that neuronatin protein has a strong predisposition to misfold and form cellular aggregates that cause cell death by apoptosis and its aggregation within cortical neurons can result in a fatal neurodegenerative disease. A better understanding of these mechanisms may open new therapeutic targets to help modify the progression of devastating neurodegenerative conditions.

Last attached article describes the role for protein tyrosine phosphatase 1B (PTP1B). This molecule plays a role in ESC differentiation - PTP1B suppresses p-ERK1/2 signaling to inhibit neural specification and promote mesendodermal commitment.

All four attached articles were published in journals with high impact factors and their citation record proves their relevance.

Dotazy oponenta k obhajobě habilitační práce (počet dotazů dle zvážení oponenta)

1.
The author says in the abstract (page 3) that she will employ her derived paradigms to generate certain types of neural cells from psychiatric patients (schizophrenia and autism) and investigate what has happened in the individual neural cell types in relation to the disorders. Could she, please, describe us the hypothesis behind this plan in more details?
2.
The author also says in the abstract (page 3) that she strongly believes that psychiatric disorders share a common causal mechanism (a defective neurodevelopmental process and synapthopathies). Could she, please, describe us what is in her opinion the role of society and social environment in the pathogenesis of psychiatric disorders?

Závěr

Habilitační práce Yuh-Man Wadeley „A quest to find out how human brain cells form and brain-related diseases develop“ ***splňuje*** požadavky standardně kladené na habilitační práce v oboru Lékařská biologie.

Praha, dne 4. 4. 2015 Doc. MUDr. Milena Králíčková, Ph.D.