UNIVERZITA PALACKÉHO V OLOMOUCI
LÉKAŘSKÁ FAKULTA

Laboratoř molekulární patologie & Ústav patologie
Hněvotínská 3
775 15 Olomouc

AKTION Česká republika - Rakousko
DZS MŠMT
Senovážné náměstí 26, Praha 1
Pošta: P.O. Box 8, 110 06 Praha 06

Věc: Závěrečná zpráva Aktion projektu č.51p19

Společně s Dr. Hannesem Neuwirtem a Dr. Fredericem Santerem děkujeme za finanční podporu našeho projektu, ke kterému přikládáme dvoustránkovou zprávu a vyúčtování z české strany.

S úctou,

V Olomouci 29.1.2009

Mgr. Jan Bouchal, PhD.
Laboratoř molekulární patologie LF UP
Hněvotínská 3
775 15 Olomouc
Tel. 585 632 462
jan.bouchal@gmail.com

Report on the Aktion project No. 51p19: ESTROGEN RECEPTOR BETA SIGNALING IN PROSTATE CANCER

Jan Bouchal [a] (supervisor Prof. Zdenek Kolar), Hannes Neuwirt [b] and Frederic Santer [b] (supervisor Prof. Zoran Culig)

[a] Laboratory of Molecular Pathology, Palacky University, Olomouc, Czech Republic

[b] Department of Urology, Innsbruck Medical University, Innsbruck, Austria

Mutual visits:

Jan Bouchal 10.9.2008 – 19.9.2008 visit in Innsbruck

Frederic Santer 4.11.2008 – 7.11.2008 visit in Olomouc

The short-term Aktion project (10.9. – 7.11.2008) helped us to finish analysis of transcriptional activity of estrogen receptor beta (ER-beta) after modulation of p300/CBP coactiovators. Knock-down of p300 and, to a lesser extent, of CBP by specific siRNAs abolished genistein stimulation of ER-beta (evaluated by luciferase assays). These results (together with the previously achieved data) were presented as a poster „COACTIVATORS p300 AND CBP ENHANCE ESTROGEN RECEPTOR BETA SIGNALING IN PC3 PROSTATE CANCER CELLS“ at the 18th Meeting of the European Society for Urological Research in Barcelona (Bouchal J., Neuwirt H., Santer FR, Culig Z, book of abstracts 61, 2008; Jan Bouchal was awarded with a travel grant from the ESUR board). We have similarly tested other prostate cancer cell lines (DU145, LNCaP, LNCaP-abl, LNCaP-IL6+ and C4-2), however, the luciferase signals were undetectable, probably due to low levels of the ER-beta and limited sensitivity of the assay.

Previously we had troubles with proliferation assays due to toxic effects of Lipofectamine 2000 on PC3 cells. We managed to enhance viability of PC3 cells by increased amount of charcoal stripped serum in the medium (from 3% to 10%) and then we observed inhibition of proliferation (and induction of apoptosis) after treatment with high doses of genistein (50 μM). However, we did not observe any significant differences in proliferation with respect to the coactivators. But, importantly, downregulation of p300 by specific siRNA sensitized PC3 cells to anti-migration effects of genistein (evaluated by scratch assays) while upregulation of p300 (by expression vector) enhanced motility of the cells even in the presence of the genistein. Importance of CBP levels for the cell motility is currently under investigation. Downregulation of p300/CBP coactivators and simultaneous treatment with genistein could be of clinical importance and upon verification our data shall be mature for publication.

Last but not least, Dr. Santer gave his lecture „Growth and apoptosis regulation in cervical and prostate cancer" at the research seminar of the Medical Faculty of Palacky University in Olomouc on 5th November 2008.

We cordially thank for the Aktion support during both projects (49p6 and its prolongation 51p19) which significantly helped us in the last stages of our study on coactivators p300/CBP and estrogen receptor beta signaling in prostate cancer.

Jan Bouchal, PhD.

and on behalf of Frederic Santer, PhD. and Hannes Neuwirt, MD. PhD.

Olomouc 26th January 2009

Vyúčtování projektu 51p19 za rok 2008

Období od	Prvek SPP	VedlPřiřazÚčt	Nákl.druh	Popis nákl.dru	Hodn./MěNO	Měna transak	Označení	Číslo ref.dokladu
9	13110021	ZAK 10	512200	Cestovné-zah	3 460,00		dr.Bouchal,Rakousko, 9.9.	1310022778
11	13110021	ZAK 10	518100	Ostatní služby	1 848,00	CZK	pobytové náklady,Dr.Santer	3010539
11	13110021	ZAK 10	518100	Ostatní služby	4 500,00	CZK	ubytování Dr.Fredereic Santer	5411004678
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UNIVERZITA PALACKÉHO v Olomouci
Lékařská fakulta
ekonomické oddělení (4)
tř. Svobody 8, P.O. BOX 159, 771 00 Olomouc 1
tel.: 585 632 054, fax: 585 223 907
IČO: 61989592 DIČ: CZ61989592