O biochemii (i nie tylko) w Beskidzie Śląskim

W dniach 20-23 września 2010 roku członkowie Studenckiego Koła Naukowego przy Zakładzie Histologii: Karolina Kociszewska, Karolina Smorzyk, Wojciech Maruszczyk i Rafał Skowronek wzięli udział w XLV Zjeździe Polskiego Towarzystwa Biochemicznego w Wiśle. Spotkanie zostało zorganizowane przez Katedrę Biochemii w Zabrzu Śląskiego Uniwersytetu Medycznego i Śląski Oddział Polskiego Towarzystwa Biochemicznego, do którego należą Wojtek i Rafał.

W Zjeździe wzięło udział ponad 1000 uczestników ze wszystkich polskich ośrodków biochemicznych. Spotkanie rozpoczęło się dwoma honorowymi wykładami: FEBS i Parnasa. Pierwszy z nich był poświęcony miozynom i molekularnym mechanizmom ruchu, natomiast drugi – białku p53 i jego białkom opiekuńczym Hsp70 i Hsp90. Organizatorzy wyodrębnili XIV sesji: Biochemia techniczna, Molekularne metody w diagnostyce i terapii nowotworów, Cytoszkielet i mięśnie, Biochemia farmaceutyczna, Molekularne mechanizmy progresji nowotworów, Biochemia roślin, Molekularne mechanizmy chorób, Mitochondria: od biochemii do medycyny, Biochemia macierzy pozakomórkowej, Biochemia antyoksydantów, Węglowodany i informacja biologiczna, Molekularna neurobiologia, Dydaktyka biochemii i Biochemia kliniczna. W tej ostatniej sesji przedstawiliśmy dwie prace (obie w formie prezentacji ustnej):

Karolina Kociszewska, Aleksandra Suszka-Świtek, Piotr Czekaj, Danuta Plewka, Katarzyna Wrona-Bogus, Aleksandra Bryzek, Danuta Kozłowska-Rup, Karolina Smorzyk, Ryszard Wiaderkiewicz
„The influence of gonadoliberin' analogs on GnRH receptor' expression in rat organs"

Rafał Skowronek, Piotr Czekaj, Aleksandra Suszka-Świtek, Danuta Kozłowska-Rup, Aleksandra Bryzek, Danuta Plewka, Ewa Czech, Wojciech Maruszczyk, Anna Wiaderkiewicz
„Do the changes in the concentration of growth hormone and ovarian hormones caused by administration of GnRH analogs modify the expression of hormone-dependent CYP3A isoforms and pregnane X receptor?".

Streszczenia wszystkich wystąpień zostały opublikowane w suplemencie oficjalnego czasopisma PTBioch: „Acta Biochimica Polonica".

Program socjalny był również starannie przygotowany i obejmował m. in. koncert skrzypcowy, uroczystą kolację oraz wspólne ognisko z góralską muzyką w tle.

Spotkanie w pięknej scenerii Beskidów było doskonałą okazją nie tylko do poszerzenia swojej wiedzy, ale przede wszystkim do wzajemnej integracji członków Koła i nawiązania nowych znajomości z badaczami z całego kraju.

Rafał Skowronek

Karolina Kociszewska i Rafał Skowronek – członkowie SKN przy Zakładzie Histologii - podczas prezentacji wyników badań.

O14.2

The influence of gonadoliberin' analogs on GnRH receptor' expression in rat organs

Karolina Kociszewska[1], Aleksandra Suszka-Świtek[2], Piotr Czekaj[2], Danuta Plewka[2], Katarzyna Wrona-Bogus[2], Aleksandra Bryzek[2], Danuta Kozłowska-Rup[2], Karolina Smorzyk[1], Ryszard Wiaderkiewicz[2]

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Gonadoliberin receptor (GnRHR) constitutes the target for GnRH-superior decapeptide of hypothalamic-pituitary-gonadal axis and for GnRH analogs receptor' agonists and antagonists, which are currently used in oncology and gynecology. Desensitization of the pituitary gland is the effect of their work, however mechanism of their action differs. It is sugessted that extrapituitary GnRHRs participate also in the creation of local axes. In the ovary GnRHR could take part in changes in the course of the cycle and evoke the ovulation preceeding pituitary stimulation
The aim of the study was to evaluate the influence of a long-term GnRH analogs administration on GnRHR mRNA and protein expression in the pituitary gland and ovary of SPD mature rat females. In the course of 1-,2- and 3-month administration of a low-dose (6ug/kg of b.w.) of GnRHR agonist (dalarelin) and antagonist (cetrorelix) and after 1,2 and 4 weeks after the end of their application, the expression of the GnRHR was evaluated immunohistochemically and by RT-PCR.
After both cetrorelix and dalarelin administration the number of cells with GnRHR expression in the anterior pituitary and pituitary pars intermedia decreased. Changes on the mRNA level confirmed changes of GnRHR protein expression. In the ovary, the number of corpora lutea containing GnRHR-positive cells considerably increased after dalarelin administration, however receptor expression kept on constant, moderate level. It was in contrast to cetrorelix-treated rats where decreasing GnRHR expression was found in granular and thecal cells of both maturing and growing follicles. All these changes were reversible.
It was concluded, that GnRHR antagonist causes partial desensitization of both hypothalamic-pituitary-ovarian and local axis, in the opposite to agonist, which inhibits only the main axis, permitting further function of ovarian axis. Desensitization caused by antagonist appears earlier comparing to agonist. Desensitization is reversible, however time of return to control values varies. Results indicate on probable interaction among GnRH, GnRHR on corticotrophes and ACTH secretion in the pituitary pars intermedia, what probably modifies either gondotropins' secretion and hypothalamic-pituitary-adrenal axis' function. Outcomes give bases to creation a new analogs' generation, which could hit only local axis. In connection of this, they could be deprived of many undesirable effects resulting from the main axis inhibition.

O14.3

Do the changes in the concentration of growth hormone and ovarian hormones caused by administration of GnRH analogs modify the expression of hormone-dependent CYP3A isoforms and pregnane X receptor?

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The expression of some drug-metabolizing enzymes, including cytochromes P450 (CYP), is sexually specific. The major regulators of sexual dimorphism of CYP expression are growth hormone (GH) and sex hormones. Temporal GH secretion is pulsatile in males and continuous in females. Therapy with analogs of GnRH (GnRH-a) results in repression of hypothalamic-pituitary-gonadal axis. Thus, the changes in levels of gonadotropins, sex hormones and — indirectly — GH, can modify the metabolism of drugs and toxins.
The aim of the study was to indicate, whether the blood changes of ovarian hormones and GH caused by a long-term administration of a new GnRH receptor' agonist — dalarelin and antagonist — cetrorelix influence the expression of hormone-dependent CYP3A cytochromes regulated by pregnane X receptor (PXR) within the liver.
SPD adult female rats were administered i. p. with dalarelin or cetrorelix (6 μg/kg of b.w.). Blood was taken after 2 and 3 months of drug administration and 1 and 2 weeks after its finishing. The concentration of GH was measured with ELISA. The concentration of estradiol, testosterone and progesterone was measured using RIA method. Expression of CYP3A1, CYP3A2, CYP3A9 and PXR within the liver acinus was analyzed immunohistochemically. Appropriate mRNAs (RT-PCR) and proteins (Western blotting) were identified and quantified by densitometry.
During the period of drug administration, dalarelin only slightly changed the level of GH, whereas cetrorelix increased the level of GH especially in the light phase of the 24-hour secretory profile. We didn't observe significant changes in the total levels of ovarian hormones. Dalarelin and cetrorelix, in a different way changed the expression, but not the localization of CYP3A isoforms within the liver. Changes of GH concentration caused by dalarelin correlated with the increase of 'male' CYP3A2/ 'female' CYP3A9 expression pattern, while changes caused by cetrorelix were correlated with the enhancement of 'female' CYP3A9 expression. These changes were poorly correlated with PXR expression.
The long-term administration of GnRH-a (especially cetrorelix) causes significant changes in the blood concentration of GH and hepatic CYP3A expressions. Effects of the therapy with GnRH-a can be potentially associated with growth disturbances in young individuals and toxic effects caused by modified CYP3A-dependent metabolism of drugs in females.