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Summary of Professional Interests and Accomplishments within the Academic and Research Work

I was born in an educated family on 2 May 1964 in Łódź. I graduated from my courses in the Faculty of Medicine at the Medical University in 1989. Having completed the postgraduate internship, I started to work in the Institute of Gynecology and Obstetrics at the Medical University in Łódź, first in the 1st Clinic of Gynecology (Head: prof. Wacław Dec), and in 1998 in the Clinic of Perinatology (Head: prof. Tadeusz Laudański). During my internship and then employment in the Institute of Gynecology and Obstetrics, I completed practice in e.g. w General Hospital in Vigo, Spain, at the Faculty of Gynecology and Obstetrics at Nijmegen University, the Netherlands and a three-month course entitled *Postgraduate Course in Gynecology and Obstetrics* in Sapir Medical Center, Meir Hospital, Kfar Saba and at Sakler Faculty of Medicine in Tel Aviw, Israel. In 1994, I passed the exam for the 1st and in 1999 for the 2nd specialisation degree in obstetrics and gynecology, both with distinctions. In 1995, I presented my thesis and in 2006 I was awarded the postdoctoral degree. Since 2002, I was an assistant professor in the Department of Perinatology, 1st Chair of Gynecology and Obstetrics at the Medical University in Łódź, and since 2006 an assistant professor with the postdoctoral degree.

In 2006–2010, appointed by the President of the Medical University in Łódź, I was a Head of the Laboratory for Medical and Environmental Pregnancy Hazards at the MU in Łódź.

In July 2008, I became an acting Head of the Perinatology Ward and in January 2010, a Head of the Perinatology Ward in M. Madurowicz Voivodeship Specialist Hospital.

From 1 January 2009 to 30 June 2009 and from 1 September 2009 to 28 February 2010 I was an acting Head of the Department of Perinatology, 1st Chair of Gynecology and Obstetrics at the Medical University in Łódź.

Since 9 July 2010 I have been employed in the Department of Perinatology, Medical University in Łódź as an Assistant Professor of the Medical University in Łódź.

Since 1 March 2010 I have been a Head of the Department of Perinatology Medical University of Łódź. At the same time, since 1 January 2010, I have been a

Head of the Perinatology Ward and the Labour Ward of M. Pirogow (formerly M. Madurowicz) Voivodeship Specialist Hospital in Łódź.

In 2015, I obtained specialisation degree in perinatology.

In 2016, I became a President-Elect of the Polish Society of Perinatal Medicine.

ACADEMIC AND RESEARCH ACTIVITY

1. Summary of the academic achievements <u>before</u> obtaining the postdoctoral degree

Before I obtained the postdoctoral degree, the total score for the published works was**: KBN/MNiSW (State Committee for Scientific Research/Ministry of Science and Higher Education) = 261, and the Impact Factor -10.823).**

I. Epidemiology of preterm deliveries and fetal malnutrition in the region of Łódź (1992-1998)

Initially, since 1991, thanks to the guidelines and encouragement from prof. Wacław Dec, and then prof. Jacek Suzin I participated actively in the research works of the Institute of Gynecology and Obstetrics, carried out together with the Environmental Epidemiology Unit of the Institute of Occupational Medicine (head: prof. N. Szeszenia-Dąbrowska). My scientific interests were devoted primarily to perinatal epidemiology, i.e. the studies of preterm delivery and fetal malnutrition risk factors, paying special attention to the effects of the so-called environmental factors. Because of its complexity and the ability to initiate effective preventive measures, this problem attracted my interest for many years. In this way I started the studies in cooperation with Wojciech Hanke, PhD, from the Epidemiology Unit of the Institute of Occupational Medicine in Łódź. The starting point for our studies was the assumption that it is necessary to obtain much information on the potential risk factors for the above, highly important pregnancy pathologies, i.e. preterm delivery and fetal malnutrition. The first aspect I decided to analyse was fetal malnutrition because of scarce data in the Polish reference works and the absence of any large population studies using contemporary epidemiological methods. The collected data and their analysis were presented in my PhD thesis in 1995, entitled "***Influence of Selected Environmental Factors on Fetal Malnutrition***" (**with distinctions**). My PhD thesis advisor was prof. Neonila Szeszenia-Dąbrowska, head of the Environmental Epidemiology Unit in the Institute of Occupational Medicine in Łódź.

The results of in-depth analyses of the material collected in the course of my studies were published in ***Ginekologia Polska*** (1996), ***Przegląd Epidemiologiczny*** (1996), ***Medycyna Pracy*** (1995) and in the ***Central European Journal of Public Health*** (1996). In the articles, I emphasized the role of such risk factors as smoking by pregnant

women, single motherhood, body-build features and place of abode (Łódź versus other towns in the region).

In 1996, a study was initiated with respect to the representative, random sample of parturients in the entire region of Łódź. **The study covered 2080 parturients in all 26 ob-gyn wards in the voivodeship of Łódź, Sieradz, Skierniewice and Piotrków.** The study was funded within the registered scope of activities of the Institute of Occupational Medicine (subject IMP 10.5) and the assistance programme PHARE. Within PHARE, the concept and methodology of the study was consulted with the epidemiologists in Belgium and the United Kingdom.

This work was aimed at **identifying risk factors for preterm delivery and fetal malnutrition, including the influence of environmental pollution, living and working conditions, exposure to tobacco smoke and other medical and socio-economic factors.** Within this project, the **model of pregnancy hazard objective assessment within the population was designed** (the study covered 2080 women) using modern epidemiological and statistical methods. The results obtained revealed that the residents of Łódź are characterised with the highest incidence of such risk factors for the incorrect pregnancy progress as smoking, single motherhood, age above 30 years and work requiring much physical effort during pregnancy. The outcomes were published e.g. in the ***International Journal of Obstetrics and Gynecology*** (1998), ***Medical Science Monitor*** (1998) and ***Human & Experimental Toxicology*** (1999), as well as in the ***American Journal of Industrial Medicine*** (1999). In cooperation with Professor Marie Saurel-Cubizolles of Institut National de la Sante et de la Recherche Medicale (INSERM) in Paris, I published an article devoted to the preterm delivery risk depending on the employment status of pregnant women *(**European Journal of Public Health (**2001*) and in ***Ginekologia Polska (**2006).*

In 1998, together with W. Hanke, PhD, I published a monograph devoted to preterm delivery and fetal malnutrition, entitled *"**Environmental Risk Factors of Preterm Delivery and Fetal Malnutrition. Study of Women in the Region of Łódź***". *Institute of Occupational Medicine, Łódź 1998:1-92*). The project deliverables were grounds for verifying the preventive and therapeutic measures aimed at reducing the percentage of preterm deliveries and fetal malnutrition.

II. "Assessment of Fetal Malnutrition Treatment Efficiency with Low Doses of Acetylsalicylic Acid"

In 1997–1998 in the Perinatology Clinic of the Institute of Gynecology and Obstetrics (together with P. Sieroszewski, PhD), I carried out a prospective study, assessing the effectiveness of fetal malnutrition treatment with small doses of

acetylsalicylic acid for the quality indexes of blood flow in the umbilical artery and in the fetal middle cerebral artery. The study results offered new insights into the **pathomechanism of fetal malnutrition sources and methods of its treatment.** The study results were rewarded at the World Congress of Perinatal Medicine in Argentina (***Kalinka J***, *Hanke W, Sieroszewski P, Laudański T, Suzin J:* ***The Effectiveness of IUGR Treatment with Low-dose Aspirin - the Effect on Birth Weight. IV World Congress of Perinatal Medicine. April 18-22, 1999, Buenos Aires, Argentina, P 131 - Poster Award - Mention of Honor).*** The work outcomes were published also in ***Ginekologia Polska*** *(*1999) and (2004). The follow-up of the said studies was the assessment of malnourished fetus treatment with acetylsalicylic acid, paying special attention to the effect of low-dose acetylsalicylic acid (1-1.5 mg/kg body weight) for the quality indexes of blood flow in umbilical vessels and the fetal middle cerebral artery. The study outcomes were published in ***Ginekologia Polska*** (2004).

III. Studies of the Effects of Environmental Exposure to Tobacco Smoke on the Course and Outcome of Pregnancy

As the data obtained from interviews do not offer a reliable assessment of the level of the passive exposure to tobacco smoke, in 1996, within the grant awarded by the State Committee for Scientific Research, in cooperation with W. Hanke, PhD, and prof. J. Suzin, I started studies using **a biological marker of nicotine, i.e. cotinine**, being a nicotine metabolite tested in the urine and serum of pregnant women.

In the prospective study, by an objective evaluation of exposure to ETS, using exposure markers, evidence was provided to prove early (20–24 week of pregnancy), adverse influence of such exposure on the blood flow indexes in the umbilical artery and related fetal malnutrition. For the first time in Poland, evidence was also provided that exposure to ETS for non-smoking pregnant women may also lead to significant reduction in newborn delivery weight. It was also confirmed that BPD parameter *(bi-parietal diameter*) in intrauterine USG examination is inversely proportional to cotinine concentration in the mother's blood. The studies confirmed the hypothesis that fetal exposure to tobacco smoke ingredients has an adverse impact on fetal growth as early as in 20–24 week of pregnancy. In the same study, I proved a significant positive relationship between S/D index (S*ystolic/Diastolic index*) and the cotinine level in the mother's serum which indicates that the mother's exposure to tobacco smoke ingredients reduces blood flow in the umbilical artery greatly which, in turn, may be one of the reasons for fetal malnutrition in mothers exposed to ETS. The works were published in: ***International Archives of Occupational and Environmental Health*** (2003), ***American Journal of Perinatology*** (2005 - with distinctions in the publication of 2006 **Year Book of Obstetrics,**

Gynecology and Women' Health; Mosby Publishing House, Elsevier Health Science, U.S.). The studies concerning the effects of environmental tobacco smoke exposure of pregnant women using **exposure biomarkers** promoted **an objective assessment of the adverse impact of smoking, including passive smoking, on *in utero* fetal growth and helped to identify the probable pathomechanism causing such changes.** The results obtained were an important support for the campaign connected with the programme called "Health and Socio-economic Policy to Reduce Tobacco Consumption", coordinated by Professor Witold Zatoński, and its outcomes were grounds for implementing interventional programmes meant to reduce adverse effects of tobacco smoke exposure during pregnancy.

IV. Bacterial Risk Factors of Incorrect Pregnancy Course and Outcome

I continued the works devoted to the risk factors of preterm delivery and fetal malnutrition within the grant from the State Committee for Scientific Research, called "**Bacterial and Non-bacterial Risk Factors of Incorrect Pregnancy Course and Outcome**" in cooperation with M. Wasiela, PhD, of the Medical Microbiology Unit at the MU in Łódź and W. Hanke, PhD, of the Environmental Epidemiology Unit, Institute of Occupational Medicine in Łódź. The study was aimed at assessing the role of bacteria found in the vagina and the endocervical canal, as well as of *bacterial vaginosis* (BV), as the risk factors of incorrect pregnancy course. That was the first time the incidence of such pathology was estimated in a random population of pregnant women at early stages of pregnancy (8–12 week). The study outcome **was a detailed identification of bacteria-related risk factors of preterm delivery (including *bacterial vaginosis*) and the determination of particular bacteria role in the preterm delivery etiology using a logistic regression model.** (***Singapore Journal of Obstetrics and Gynecology*** (2004); ***Med. Dośw. Mikrobiol***. (2004) ***Polish Journal of Gynaecological Investigations*** (2002) and ***Med. Dośw. Mikrobiol***. (2003).

The study helped also to identify the relationship between environmental factors, including tobacco smoking and the incorrect bacterial flora in lower reproductive tract during pregnancy (***Medical Science Monitor*** 2001) and ***Journal of Perinatal Medicine*** (2002). (***Fetal Diagnosis and Therapy*** 2003). Identification of the environmental risk factors of incorrect bacterial flora in pregnant women contributed to the explanation of the observed differences in BV incidence in various populations and is likely to reduce the said incidence in our population, by eliminating the modifiable factors, and consequently, reduce the number of preterm deliveries. The work outcomes helped to understand the mechanisms causing preterm delivery and low delivery weight of newborns.

V. Assessment of Proinflammatory Cytokine Level in Vaginal Fluid of Pregnant Women as the Early Marker of Preterm Delivery

In accordance with the outcomes of previous studies, one of the most important factors leading to preterm delivery is inflammation of reproductive tract, caused e.g. by incorrect bacterial flora. The mechanisms causing obstetric complications related to the reproductive tract infections have not been examined sufficiently so far. For this reason, the objective of my subsequent project, carried out in cooperation with M. Wasiela, PhD, of the Medical Microbiology Unit of the MU in Łódź and prof. E. Brzezińska-Błaszczyk of the Experimental Immunology Unit, MU in Łódź, was the quantitative assessment of selected cytokines (IL-1 alpha, IL-1 beta, IL-6, IL-8) in the cervicovaginal discharge of pregnant women (in reference to environmental, medical and microbiological factors) as an early marker of preterm delivery. In 2001–2003 I performed a prospective study of 121 pregnant women between 21^{st} and 36^{th} week of pregnancy.
It helped to determine the relationship between bacterial infections and the concentration of the studied cytokines. It was discovered e.g. that *bacterial vaginosis* (BV) significantly increased the concentration of IL-1 beta (BV –74.55 pg/mL vs. 19.8 pg/mL for women with correct flora) and IL-1 alpha (BV-110.2 vs. 33.5 pg/mL) and to a negligible degree increased IL-8 concentration (539.6 vs 473.7 pg/mL respectively). No relationship was detected between BV and IL-6 concentration. The effect of infection caused by *Mycoplasma hominis* and *Ureaplasma urealyticum* on the concentration of the studied cytokines in the vaginal fluid of pregnant women was determined (***Medycyna Doświadczalna i Mikrobiologia***, 2004) and ***Medycyna Doświadczalna i Mikrobiologia***, 2005).

The analysis of relationship between the selected cytokine concentration in the cervicovaginal discharge and the preterm delivery ***in the group of women with incorrect bacterial flora in lower reproductive tract*** during pregnancy revealed significant increase in preterm delivery risk for women with low concentrations (< 25%) of IL-1 alpha and IL-8, and a similar tendency for low concentrations of IL-6 and IL-1 beta. The studies confirmed cytokine assessment fitness for *early* assessment of the preterm delivery risk in the group of pregnant women with incorrect bacterial flora. The study results identified for the first time which women with pathological vaginal flora in pregnancy are exposed to a particular threat of preterm delivery and indicated the mechanism causing such premature birth for those women. Low concentrations of certain cytokines in pregnant women with incorrect bacterial flora in the lower reproductive tract may promote development of infections taking place during pregnancy and, consequently, increase the risk of preterm delivery (***Ginekologia Polska,*** 2003); ***Ginekologia Polska*** (2005) and ***Kalinka J***, *Sobala W,*

Wasiela M, Brzezińska-Błaszczyk E: Decreased Proinflammatory Cytokines in Cervicovaginal Fluid, as Measured in Midgestation, are Associated with Preterm Delivery. ***American Journal of Reproductive Immunology****. 2005*). I confirmed also that the identification of cytokines in cervicovaginal fluid of pregnant women offers an early prognosis of the congenital infection of newborns (***Kalinka J. et al. Journal of Perinatal Medicine; 2006***). Lower concentrations of IL-1 beta, IL-6 and IL-8 were found during gestation of women giving birth to children with an intrauterine infection **(*Journal of Pediatrics and Neonatology*,** 2005).

The result of the continued studies following the award of my postdoctoral degree and of the cooperation with scientists of **Vanderbilt University, U.S.** was the identification of the correlation between the concentration of the studied cytokines and selected parameters (gestational age, mother's age, BMI, pH) in the group of pregnant women with BV and *Mycoplasma hominis* infection *(Ryckman KK, Williams SM,* ***Kalinka, Journal of Reproductive Immunology; 2008***). The results offer an improved understanding of the immunological response mechanisms to bacterial infections in the lower reproductive tract of pregnant women.

ACADEMIC AND RESEARCH ACTIVITY

2. Summary of the academic achievements <u>after</u> obtaining the postdoctoral degree

Having obtained the postdoctoral degree, my total score for the published works was KBN/MNiSW = 595, and the Impact Factor - 42.105, including 27.897 as the first author).

VI. Assessment of the Progesterone, Estradiol, PIBF (Progesterone-induced Blocking Factor) and Selected Cytokines in Blood Serum of Women with Threatened Miscarriage, Treated with Dydrogesterone and of Women with the Correct Progress of Early Pregnancy

The subject was studied in the Perinatology Clinic, commenced before and continued after obtaining the postdoctoral degree, **study director: J. Kalinka MD PhD** in cooperation with **prof. Julia Szekeres-Bartho of the Department of Medical Microbiology and Immunology, Pecs University, Medical School, Hungary and Reproductive and Tumor Immunology Research Group of the Hungarian Academy of Sciences.**

The threatened abortion is a clinical condition indicating troubled physiological course of pregnancy. There is still much controversy concerning the methods and effectiveness of medication for threatened abortions. Besides the causal treatment of the mother's diseases and surgical correction of reproductive organ defects, the administration of progesterone derivatives in the 1st gestation trimester is the most important method of treating threatened miscarriage. Not all scholars accept the legitimacy of using progesterone derivatives to treat threatened abortion. The new light was shed on the progesterone role and the protective effect mechanism on the developing fetus by the experimental studies of e.g. Professor Szekeres-Bartho, according to which in the presence of progesterone lymphocytes of pregnant women release PIBF protein, assisting in the modulation of immunological mechanisms preventing miscarriage.. The study results prove that low PIBF level is correlated with IL-12 interleukin increase and is characteristic of preterm pregnancy end. Moreover, PIBF inhibits the activity of NK cells and has an antiabortion effect in mice by reducing the activity of NC *(natural cytotoxic*) cells. The immunological pregnancy protection results from the progesterone effect, while the progesterone protective effect mechanism is based on cytokine production control. If PIBF level is low, Th-1 cytokine becomes predominant and, consequently, pregnancy is terminated before due date.

The outcomes of our study were the first worldwide to prove that PIBF level in the urine of women experiencing threatened abortion is significantly lower than in the urine of healthy women. Dydrogestrone (progesterone derivative) supplementation caused increased PIBF values when compared to the ones observed in the reference group. No significant difference in Th1 and Th2 cytokine concentrations where detected in both groups which means that the major problem related to threatened abortion is endocrine disorders and not immunological ones. **Reduced PIBF level may be a pathomechanism causing miscarriage and its assessment may help to diagnose further gestation progress at an early stage.** The study results were published in the ***American Journal of Reproductive Immunology*** (***Kalinka J***, *Szekeres-Bartho J: The Impact of Dydrogesterone Supplementation on Hormonal Profile and Progesterone-induced Blocking Factor Concentrations in Women with Threatened Abortion*. ***American Journal of Reproductive Immunology***. *2005),* ***Kalinka J***, *Radwan M: The Impact of Dydrogesterone Supplementation on Serum Cytokine Profile in Women with Threatened Abortion.* ***American Journal of Reproductive Immunology***. 2006) and ***Kalinka J***, *Szekeres-Bartho J: Physiology Should be Supported with Evidence in Progesterone Administration for Threatened Miscarriage - Authors' Reply.* ***American Journal of Reproductive Immunology.*** *2005).*

The publication of works concerning the influence of immunological factors on early pregnancy (***Kalinka J***, *Radwan M: The Impact of Dydrogesterone*

Supplementation on Serum Cytokine Profile in Women with Threatened Abortion. American Journal of Reproductive Immunology. 2006 and ***Kalinka J,*** *Szekeres-Bartho J: Physiology Should be Supported with Evidence in Progesterone Administration for Threatened Miscarriage - Authors' Reply. American Journal of Reproductive Immunology. 2005)* resulted in my invitation, in 2007, to give a lecture entitled "***The Role of the Immunological Factors in Early Pregnancy Failure and in Preterm Delivery***" during the ***International Workshop on Air Pollution and Human Reproduction. GSF-National Research Center for Environment and Health, Institute of Epidemiology in Munich, Germany.*** The outcome of this international cooperation was the report on the broad effect of the environment on reproduction, including e.g. the results of my works, and published in the ***Environmental Heath Perspectives*** **(IF=6.123*)*** *in* ***2008***. (*Slama R, Darrow L, Parker J, Woodruff T, Strickland M, Nieuwenhuijsen M, Glinianaia S, Hoggatt J. K, Kannan S, Hurley F,* ***Kalinka J,*** *Sram R, Bauer M, Wilhelm M, Heinrich J, Ritz B: Atmospheric Pollution and Human Reproduction: Report of the Munich International Workshop*). The significance of the balanced Th1 and Th2 cytokine production for correct gestation and the modulatory role of progesterone on Th1/Th2 cytokine production, as well as the detailed description of progesterone activity mechanism in women with threatened abortion, recurrent miscarriage and preterm delivery were presented in two review articles (*Raghupathy R,* ***Kalinka J****: Cytokines Imbalance in Pregnacy Complications and its Modulation.* ***Frontiers in Bioscience****.* ***2008*** *and Szekeres-Bartho J, Wilczynski JR, Basta P,* ***Kalinka J****: Role of Progesterone and Progestin Therapy in Threatened Abortion and Preterm Labour.* ***Frontiers in Bioscience. 2008;*** **IF=2.72)**

VII*. "****Assessment of the Relationship between the Polymorphism of Genes Encoding Selected Proinflammatory Cytokines and the Preterm Labour***, no. 502-11-363; **subject director**: **Jarosław Kalinka MD PhD**

The preterm delivery etiology is complex and not fully explained. Epidemiological studies reveal that preterm delivery depends not only on medical and environmental factors, but may also be genetic. There is evidence proving the relation between the concentration of certain cytokines (IL-1, IL-6 and TNF alpha) in the amniotic fluid and the cervicovaginal fluid in pregnant women and the risk of preterm delivery (***Kalinka J et al. Decreased Proinflammatory Cytokines in Cervicovaginal Fluid, as Measured in Midgestation, are Associated with Preterm Delivery. Am J Reprod Immunol. 2005)***. This is why genetic examinations were initially focused on the analysis of polimorphism in genes encoding selected inflammatory mediators, the roles of which in the preterm delivery pathogenesis had already been proved. The studies were carried out in the Molecular Biology Unit,

Chair of Oncology at the Medical University in Łódź. DNA was isolated from peripheral blood lymphocytes using Higuchi's method. The studied population comprised 125 women altogether, including: 62 women with preterm delivery (study group) and 63 women with timely delivery (> 37 week of pregnancy), i.e. the reference group.

No significant differences in the incidence of particular genotypes (IL1β+3953*1, IL1β+3953*1/ IL1β+3953*2 i IL1β+3953*2) were confirmed between the group of women with preterm delivery and the ones with timely delivery. No significant differences in the incidence of particular genotypes (CC, GC and GG) were confirmed between the group of women with preterm delivery and the ones with timely delivery. The polymorphism of TNF gene promoterα (-308): in the group of women with preterm delivery, TNF genotypeα*1 (72.6%) was most frequent, and TNFα*2 (1.6%) the least frequent. In the group of women with timely delivery, TNFα*2 genotype was 3 times more frequent: -5.5%.

The analysis of alleles in 2nd intron of IL1RN gene revealed that the most frequent variant in the group of women with preterm delivery is IL1RN*1/IL1RN*1, found in 37.1% of the examined women when compared to 54.7% in the group of women with timely delivery (p=0.05). On the other hand, IL1RN*1/IL1RN*2 was significantly more frequent in women with preterm delivery (45.2%) when compared to the ones with timely delivery (30.2%). **The presence of IL1RN*1/IL1RN*1 allele was an important preventive factor for the preterm delivery OR=0.49 (0.22-1.01**), **while the presence of IL1RN*1/IL1RN*2 allele was an important risk factor for the preterm delivery.** (***Kalinka J:*** *Selected Cytokines Gene Polymorphisms and the Risk of Preterm Delivery in the Population of Polish Women. XXI European Congress of Perinatal Medicine, Istanbul, Turkey, September 10-13, 2008.* ***The Journal of Maternal-Fetal Medicine&Neonatal Medicine. 2008;21, Suplement 1: 119; Kalinka J****, Bitner A: Ocena związku polimorfizmów genów kodujących wybrane cytokine z występowaniem porodu przedwczesnego w populacji kobiet polskich [Assessment of the Relationship between the Genes Encoding Selected Cytokine with the Preterm Delivery in the Population of Polish Women].* ***Ginekologia Polska****. 2009, 80: 111-117.* ***KBN=10).***

The studied polymorphisms were compared in the group of women with preterm delivery with the premature rupture of membranes (PPROM) and without PPROM. 1β (IL1β+3953) interleukin gene polymorphism: genotype IL1β+3953*1 was more frequent in women with preterm delivery and PPROM (56.3%) when compared to 46.6% in the group without PPROM. On the other hand, the genotype IL1β+3953*1/ IL1β+3953*2 was more frequently detected in the group of women with preterm delivery without PPROM 53.3% when compared to 37.5% of women with preterm delivery with PPROM. 6 (IL6 -174G/C): interleukin gene promoter polymorphism: In the group of women with preterm delivery with PROM, the CC

genotype was 2x more frequent than in the group without PROM (40.6% vs 20.0%), while GC was more frequently detected in the group without PROM (53.3% vs 31.3%). The polymorphism of TNF gene promoterα (-308): no significant differences of incidence between the particular genotypes (TNFα*1, TNFα*1/TNFα* 2 and TNFα*2) were detected for the studied group. The analysis of alleles in 2nd intron of IL1RN gene revealed that IL1RN*1/IL1RN*1 variant was more frequent in women with preterm delivery with PROM than in the ones without PROM (43.8 vs 30.0%). The studied polymorphisms in the group of women with preterm delivery with PROM where compared to the parameters for women with timely delivery. IL1RN*1/IL1RN*2 was found significantly more often (p=0.09) in women with preterm delivery with the premature rupture of membranes (40.6%) when compared to 30.2% in the group of women with timely delivery. The results may suggest different genetic predispositions for preterm delivery in women with the premature rupture of membranes (PROM).

The determination of the relationship between the polymorphism of genes encoding selected cytokines and the risk of preterm delivery in a given population may enable to identify women exposed to the risk of giving birth to a premature newborn at an early stage and contribute to reducing preterm deliveries and their negative effects. (***Kalinka J***, *Bitner A: Interleukin-1β and Interleukin -1 Receptor Antagonist Genes Polimorphisms and the Risk of Spontaneous Preterm delivery in the Population of Polish Women.* ***Archives of Perinatal Medicine****. 2008) and;* ***Kalinka J***: *Genetic Predispositions to Preterm Delivery. 5th Congress of the Polish Society of Perinatal Medicine "Perinatology in 21st Century" Łódź, 25-27 June 2009: 16).*

Within the activities of PREBIC group, I became a member of **PREGENIA** i.e. ***Preterm Birth and Genetics International Alliance***, **U.S.** and an active participant of international studies devoted to genetic predispositions to preterm delivery within the ***Preterm Birth Genome Project Consortium, U.S.***

VIII . ***"Epidemiology of Reproductive Threats in Poland - Multicenter, Prospective Cohort Study".*** The project commissioned by the Ministry of Science and Higher Education no. PBZ-MeiN-8/2/2006, (agreement no. K 140/P01/2007/1.3.1.2).

Study task **"*Assessment of the Selected Cytokine Concentration in Cervicovaginal Fluid of Pregnant Women as an Early Risk Indicator of Pregnancy Pathology*".**
Study task director: Jarosław Kalinka MD, PhD

The etiology of preterm birth (PTB) is composed of numerous factors, but its major cause, likely to be responsible for about 25-40% PTB, is believed to be an intrauterine infection. The mechanism, as a result of which pathogens entering the amnion space initiate preterm uterine activity, may be shortly described as follows: The Toll-like

receptors 4 (TLR4) expressed on the immune system cells recognise lyposaccharides (LPS), i.e. components of bacterial cell wall. LPS connection to TLR4 activates a nuclear factor-κβ (NF-κβ) which, in turn, stimulates the maternal, fetal and placental tissues to produce numerous cytokines, e.g. interleukin-1β (IL-1β), tumour necrosis factor-α (TNF-α), interleukin-6 (IL-6), interleukin-18 (IL-18). The release of the above cytokines affects prostaglandins production which, in turn, leads to uterine activity, contributing to PPROM and/or preterm delivery. The pathogenesis of preterm delivery in the intrauterine infection dependent mechanism involves also anti-inflammatory cytokines, i.e. interleukin-10 (IL-10) and interleukin-1 receptor antagonist (IL-1ra), encoded by IL1RN gene, as well as interleukin-15 (IL-15), controlling activation and proliferation of T lymphocytes and NK cells. In numerous works it was proven that individuals may differ in terms of cytokine concentration produced in response to infectious factors and also with respect to the expression of proteins involved in immunological response, including with respect to TLR4 expression on the cell membrane surface of immune system cells. The differences may result e.g. from the polymorphism of genes encoding the said cytokines and TLR4. It was proved that the presence of those polymporphous alleles is related to the smaller TLR4 expression on the surface of the immune system cells (this is connected probably with the changed configuration of the extracellular receptor domain, impairing its transmembrane transportation) and, consequently, smaller ability to activate NF-κβ and IL-1. Considering the said information, and also that the intrauterine infection is one of the major preterm delivery causes, it can be assumed that the pro- and anti-inflammatory cytokine concentration in the cervicovaginal fluid may be different in women with preterm delivery and in women with timely delivery and also that the maternal and fetal presence of polymorphous alleles of the genes discussed above may increase or decrease the preterm delivery risk **The study objectives included:**

- assessment of the relationship between IL-1β, IL-6, IL-10, IL-15 and IL-18 concentration in the cervicovaginal fluid taken from women with threatened preterm delivery between 22nd and 34th week of pregnancy and the risk of preterm delivery;

- assessment of the relationship between the maternal presence of polymorphic alleles: IL1β (+3953C>T), IL6 (-174G>C), TNFα (-308G>A), IL1RN and TLR4 (896A>G, 1196C>T) and the risk of preterm pregnancy termination;

- assessment of the relationship between the fetal presence of polymorphous alleles IL1β (+3953C>T), IL6 (-174G>C), TNFα (-308G>A), IL1ra and TLR4 (896A>G, 1196C>T) and the risk of preterm delivery;

- assessment of the gene - gene interaction effect on the risk of premature birth.

The results obtained revealed that **IL-6** concentration in the cervicovaginal fluid between 22nd and 34th week of pregnancy, reaching above **100pg/mL was connected with more than two and a half times increase in giving birth to a premature newborn**.

Polymorphism and the preterm birth (PTB). No statistically significant effect of the *maternal* presence of the polymorphous allele TNF alpha, IL-6 and IL1β*2 on the risk of delivery before 37th, 33th week of pregnancy and preterm delivery as a result of premature rupture of membranes was proven. **However, the statistically significant effect of the maternal presence of at least one polymporphous allele IL1RN*2 on the risk of giving birth to a child before 33rd week of pregnancy was proven.** Analysing the effect of the maternal presence of the polymporphous allele **TLR4(1196C>T)** on the risk of birth before 33rd week of pregnancy, its statistically significant **protective influence** was detected. Heterozygous women **(1 wild allele, 1 TLR4(1196C>T))** had about **3.5 times lower risk of giving birth to a premature child before 33rd week of pregnancy.** It was also proved that the simultaneous presence of at least 1 polymorphous allele **TLR4 896A>G** and at least 1 polymorphous allele **TLR4 1196C>T** is related to the statistically significant **reduction of the risk of preterm delivery before 33rd week of pregnancy.** For the first time in Poland, the effect of the *fetal presence* of the polymporphous allele TLR4 (896A>G) and allele TLR4(1196C>T) on the preterm delivery risk was assessed. No statistically significant effect of the presence of those alleles on the risk of delivery before 37th, 33th week of pregnancy or preterm delivery as a result of premature rupture of membranes was proven. The study revealed also that the simultaneous maternal presence of the adverse TLR4 (1196CC) genotype with at least one adverse IL1RN*2 allele brings about statistically significant increased in the preterm delivery risk before 33rd week of pregnancy, OR=4.1 (1.57-10.68). On the other hand, the simultaneous maternal presence of the protective TLR 4(1196CT) genotype with the adverse IL1RN*2 genotype, as well as the presence of the adverse TLR4 (1196CC) genotype with the favourable IL1RN*1 genotype, was not connected with any change in the preterm delivery risk. **The data confirm a significant influence of the gene - gene interaction on the preterm birth risk**. The outcomes were published e.g. in ***Ginekologia Polska. 2009***, ***Archives of Perinatal Medicine. 2008***; ***J Archives of Medical Science. 2010***, *and in* ***American Journal Reproductive Immunology in 2013.*** **(***Bitner A, Sobala W,* ***Kalinka J****. Association Between Maternal and Fetal TLR4 (896A>G, 1196C>T) Gene Polymorphisms and the Risk of Pre-term Birth in the Polish Population).* The outcomes were also presented many times at conferences, e.g.*: 1)* ***Kalinka J****: Selected Cytokines Gene Polymorphisms and the Risk of Preterm Delivery in the Population of Polish Women. XXI European Congress of Perinatal Medicine, Istanbul, Turkey, 2008. 2)* ***Kalinka J****: An Association between Selected Cytokine Gene pPolymorphisms and the Risk of*

Preterm Delivery in the Population of Polish Women. XXI European Congress of Perinatal Medicine, Istanbul, Turkey, 2008. 3) ***Kalinka J,*** *Bitner A: Selected Cytokine Gene Polymorphisms and the Risk of PPROM followed by Preterm Delivery in the Population of Polish Women. Abstracts of XIX FIGO World Congress of Gynecology and Obstetrics, Cape Town, South Africa, 2009 and* ***Kalinka J,*** *Bitner A: Interleukin-1 and Interleukin-1 Receptor Antagonist Genes Polimorphisms and the Risk of Preterm Labour in the Population of Polish Women. Book of Abstracts. XXII European Congress of Perinatal Medicine. Granada, Spain, 2010.)*

The summary of the state-of-the art knowledge on the influence of genetic factors on the spontaneous preterm delivery was included in the chapters of the following handbooks: (***Kalinka*** *J, Bitner A:* ***Genetyczne uwarunkowania porodu przedwczesnego. Ciąża wysokiego ryzyka [Genetic Predispositions to Preterm Delivery. High-risk Pregnancy].*** *Editor Grzegorz H. Bręborowicz. Third edition, updated and extended. Ośrodek Wydawnictw Naukowych. Poznań MMX. ISBN 83-7314-059-2: 2010: 155-162 and* ***Kalinka J****, Bitner A:* ***Poród przedwczesny [Preterm Delivery]****. 1-38. PZWL Edited by Grzegorza H. Bręborowicza. 2015, 1-38*).

IX. ***"Prevention of Incorrect Uterus Contraction and Bleeding following Cesarian Cut with Carbetocin (Pabal)"*** The project was carried out in the Perinatology Clinic at the Medical University in Łódź. 2007-2012**. Study director: Jarosław Kalinka MD, PhD**

The project objective was to estimate the said preventive method against the routine preventive recommendations in postpartum bleeding and uterine contraction disorders following cesarean cuts. The study covered patients administered carbetocin as a postpartum bleeding prevention following a cesarean cut. The results show that when the carbetocin was administered, the uterine contraction corresponding to many-hour oxytocin administration, reduced intraprocedural bleeding and small reduction in the blood count values following the procedure were obtained.

The single 100 μg carbetocin dose administered intravenously turned out efficient to prevent postpartum bleeding in women following a cesarean cut and also in the group of women with high risk of postpartum bleeding (***Kalinka J****: Ocena skuteczności stosowania karbetocyny (Pabalu) w profilaktyce krwawień poporodowych u kobiet po cięciu cesarskim – doniesienie wstępne [Efficiency Assessment of Carbetocin (Pabal) Administration to Prevent Postpartum Bleeding in Women following a Cesarean Cut - Preliminary Findings].* ***Ginekologia Polska. 2009***). It is of utmost importance that the administration of carbetocin helped to prevent peripartum bleeding following

cesarean cuts in emergency **(*Kalinka J et al. Ginekologia i Położnictwo Medical Project. 2009).*** The obtained outcomes contributed to the development of the **opinion of the experts of the Polish Gynecological Society (PGS)** concerning the preventive and therapeutic carbetocin administration in obstetrics (*Poręba R, Oszukowski P, Oleszczuk J, Bręborowicz G, Wielgoś M, Czajkowski K, Smolarczyk R, **Kalinka J**: Opinion of the Expert Team of the Polish Gynecological Society concerning Carbetocin Administration to Prevent Postpartum Bleeding - Knowledge as at 2012. **Ginekologia i Położnictwo Medical Project.** 2012, 2: 56-58 and the extended opinion of PGS experts published in 2013* ***(GinPolMedProject.** 2013;1(27): 41*) and to my invitation to participate in the international meeting of the expert team, devoted to the preventive carbetocin administration aspects to prevent peripartum bleeding in women giving birth vaginally - Paris, 2013.

In 2016, the results of the multi-center study where presented which proved that carbetocin administration to prevent uterine atony following birth by cesarean cut entails lower hospital costs when compared to the standard preventive methods (oxytocin). (***Ginekologia Polska**. 2016*) and also at *ISPOR 21st Annual International Meeting. Washington DC, U.S. 2016 and at XXV European Perinatal Congress. Maastricht.* 2016.

X. ***Assessment of the Immune System Cell Activity Changes in Endometrium during a Physiological Menstrual Cycle, in Decidua in Physiological Conditions and in Pathological Conditions Complicating Pregnancy, as well as in the Endometriosis Centres and in Ovarian Tumour"*** **No. 0888/B/P01/2008/35**

Director prof A. Basta, Clinic of Gynecology and Oncology Collegium Medicum of the Jagiellonian University;

Executed by Jarosław Kalinka MD PhD, Department of Perinatology, the Medical University in Łódź

The project objective was to determine the effect of endometrium/decidua during labour and what molecular changes in the endometrium/decidua which be observed during the labour and are likely to be responsible for hindered activity of immune cells during labour. This programme is a part of the year-long study devoted to the explanation of the molecular background of the mother's immune tolerance to fetal antigens. One of processes of key importance for that phenomenon is the inhibition of the mother's immune cell activity. This is understandable in the case of the lasting tolerance process while during labour the increased activity of the

mother's immune cells is observed. As the immune tolerance is created by the mother and the fetus together, the changes in the mother's immune system, endometrium and trophoblast cells are crucial for that process. The studies were aimed at identifying the regulatory immune cells in the endometrium/decidua during labour as well as assessing their activity, with detailed phenotype characteristics of those cell populations. For the examination, the following cells were selected: Treg (lymphocytes CD4+CD25+FOXP3) and macrophages CD14+B7H4+, out of all cells participating in that process. The macro environment condition was assessed by examining expression of proteins inhibiting immune cells on endometrium cells, i.e. RCAS1 and HLA-G. The studies devoted to identifying Treg lymphocytes in peripheral blood during labour enabled to prove the reduced population of those immune cell group during the labour initiation. Most probably, this is one of mechanisms responsible for changes in the mother's immune tolerance to fetal antigens observed during labour. The reduced number of TReg lymphocytes may result in increased cytotoxic response of the mother. The studies of RCAS1 antigen immunoreactivity in decidua and of the soluble form of this antigen in the mother's peripheral blood during labour, pre-eclampsia and missed abortion enabled to confirm the participation of the said antigen in creating the mother's immune tolerance to fetal antigens. They also indicate the possibility to detect the changes in tolerance level by assessing expression of that antigen. As the antigen is responsible for selective inhibition of NK cells and T lymphocytes, the changes in its expression during pre-eclampsia, labour finished with cesarean cut or ongoing miscarriage confirm the increased cytotoxic activity of the mother's immune system in the said circumstances. The background factor of those processes is the increased activity of mononuclear cytotoxic cells of the mother's immune system.

The results were published in the following: 1). *Gałązka K, Wicherek Ł, Pityński K, Kijowski J, Zając K, Bednarek W, Dutsch-Wicherek M, Rytlewski K,* ***Kalinka J****, Basta A, Majka M. Changes in the Ssubpopulation of CD25+ CD4+ and FOXP3+ Regulatory T Cells in Decidua with Respect to the Progression of Labor at Term and the Lack of Analogical Changes in the Subpopulation of Suppressive B7-H4 Macrophages - a Preliminary Report.* ***Am J Reprod Immunol*** *2009;61:136-46. 2). Wicherek Ł, Basta P, Gałązka K, Mak P, Dancewicz L,* ***Kalinka J****. RCAS1 Decidual Immunoreactivity and RCAS1 Serum Level during Cesarean Dection with Respect to the Progression of Labor.* ***Am J Reprod Immunol*** *2008;59:152-158. 3). Gałązka K, Wicherek Ł, Sikora J, Czekierdowski A, Banaś T, Bednarek W, Obrzut B, Blecharz P, Reroń A,* ***Kalinka J****. RCAS1 Decidual Immunoreactivity during Stillbirth: Immune Cell Presence and Activity.* ***Am J Reprod Immunol*** *2008 Dec;60(6):513-22. and 4). Wicherek Ł, Basta P, Sikora J, Gałązka K, Rytlewski K, Grabiec M, Lazar A,* ***Kalinka J.*** *RCAS1 Decidual Immunoreactivity in Severe Pre-eclampsia: Immune Cell Presence and Activity.* ***Am J Reprod Immunol*** *2007;58:358-366.*

X. "*Assessment of the Association between Vitamin D Concentration in the Blood Serum of Parturients and the Pregnancy Duration, Including the Effect of Selected Genetic Factors"* Grant of the National Science Centre - Preludium 4

Number: UMO-2012/07/N/NZ5/01720 2013-.2016

Patron/Advisor: **Jarosław Kalinka MD PhD**

Project Director**:** Marta Baczyńska-Strzecha

The studies assessing the impact of genetic factors on the preterm delivery were followed up with the project aimed at determining the association between vitamin D concentration in the blood serum of parturients, including the presence of a specific genetic variant of vitamin D receptor (VDR) (polymorphisms of FokI, ApaI, TagI and Bsml), and the pregnancy duration. The study assessed also the incidence of particular genetic variations of VDR receptor in the Polish population. It was discovered that the presence of the rarer FokI ff genotype in pregnant women is connected with preterm delivery risk reduced by 63%, whereas the presence of isolated VDR polymorphisms, i.e. Taq1, Bsm1, Apa1 does not affect the preterm delivery risk. The presence of rare genotype combinations, i.e. Bb/AA/Tt i BB/Aa/tt, may also reduce the preterm delivery risk (*Baczyńska-Strzecha M, **Kalinka J**: Influence of Apa1 (rs7975232), Taq1 (rs731236) and Bsm1 (rs154410) Polymorphisms of Vitamin D Receptor on Preterm Birth Risk in the Polish Population. – **Ginekologia Polska**. 2016 and Baczyńska-Strzecha M, **Kalinka J:** Assessment of a Correlation Between a Vitamin D Level and Prevalence of Preterm Births in the Population of Pregnant Women in Poland. - **International Journal of Occupational Medicine and Environmental Health**, article accepted for publication in 2017).* The results were presented also at the world congress*: (Baczynska-Strzecha M, **Kalinka J**: Correlation between Parturients` serum vitamin D Level and Duration of Pregnancy in Polish Population. and Baczynska-Strzecha M, **Kalinka J:** Correlation between Parturients` VDR Fok1 Polymorphism (rs2228570) and Duration of Pregnancy in Polish Population. Abstracts from the ISGE World Congress 2016. 17th World Congress Gynecological Endocrinology, 2-5 March, Firenze, Italy. Gynecological Endocrinology 2016.* (**Award for the Project Director** for the said work in the competition for scholars below 34 years of age by the ***International Society of Gynecological Endocrinology (ISGE*)**.

XI. "**Assessment of the Molecular Mechanisms at the Interface between a Human Body, Pathogens and Environmental Factors (InterMolMed)". Task 2, called "Identification of Molecular Mechanisms of Viral Infections and Non-specific**

Congenital Immunity, as well as New Therapeutic Shields and Anti-viral Agents. Medical Experiment within the Research Project of the Innovative Economy Programme no. POIG.01.01.02-10-107/09. 2012-2014

Scientific cooperation: Jarosław Kalinka MD PhD

Task 2 Director: prof. Zbigniew J. Leśniewski, Medical Biology Institute, Polish Academy of Sciences

The study was aimed at determining the expression levels for genes encoding TLR1-10 receptors, belonging to the group of pattern recognition receptors (*PRR)*, in timely placenta of non-complicated pregnancies and examining the effects of the experimental infection with laboratory strains of HCMV, HSV-1 i VSV on TLR expression level. Thanks to the intense development of studies devoted to PRR, the task carried out within this project was extended with pioneer studies of RIG-I-like receptor expression (RIG-I, MDA5, LGP2). The clinical specimens for examination were human placentas (38th-40th week of pregnancy), received following the delivery. The research model employed was the tissue sections from the maternal and the fetal part of placenta. Relative mRNA expression level for PRR encoding genes was identified in RNA isolates, derived from the placenta not infected and from the ones infected with HCMV in vitro. The expression was studied using PCR method in real time, with YWHAZ as a reference gene.

It was observed that human placenta tissues from non-complicated pregnancies reveal expression of genes encoding all Toll-like receptors 1-10, with the age of organ cultures exerting a significant influence on TLR expression level. The lowest expression level in the studied organs was displayed by TLR3 in the maternal and fetal parts of organs. Experimental infections of placenta with HSV-1, HCMV or VSV did not significantly affect the change in TLR1-10 expression. In timely placenta, expression of RIG-I, MDA5 and LGP2 was found at mRNA level. The highest level of expression in tissues infected with HCMV and not infected was displayed by the gene encoding LGP2 receptor, while the lowest one - MDA5. A significant increase in RIG-I expression was observed in placentas infected with VSV which confirms involvement of the said receptor in the recognition of the viral dsRNA. For selected placenta, expression (IFNß, TNFα) and production (IFNα, TNFα, IL6, IL8) of selected cytokines were identified. The preliminary results were presented at: (*Suski P., **Kalinka J**., Studzinska M., Jablonska A., Lesnikowski Z.J., Paradowska E. Expression profiles of Toll-like Receptors 1-10 in Human Placenta during Viral Infection. and Jabłońska A., Suski P., Studzińska M., **Kalinka J**., Leśnikowski Z.J., Paradowska E. Expression of Retinoic Acid-inducible Gene I (RIG-I)-like Receptors (RLRs) in the Human Term Placenta. 15th International Conference of Immunology (ICI), August 22-27, 2013, Milan, Italy). P4.01.078. Frontiers of Immunology. Conference Abstract: 15th International*

*Congress of Immunology (ICI). doi: 10.3389/conf.fimmu.2013.02.00293. p. 554) and also (Jabłońska A., Paradowska E., Studzińska M., Suski P., **Kalinka J.,** Leśnikowski Z.J. Expression of RIG-I-like receptors in human placentas. and Suski P., Paradowska E., Studzińska M., Jabłońska A., **Kalinka J.,** Leśnikowski Z.J. Infection with HCMV, HSV-1 or VSV in in vitro conditions versus mRNA expression for Toll-like receptors in human term placenta. I Congress of the Polish Virology Society, June 19-22, 2013, Lublin. Conference materials. I-4).*

PENDING SCIENTIFIC STUDIES:

XII. Grant of the National Science Centre OPUS7 No. 2014/13/B/NZ7/02317 entitled "Risk Factors for Congenital and Postnatal Infections with Cytomegalovirus". 2015-2018.

Performed by: Jarosław Kalinka MD PhD

Project director: Edyta Paradowska, Professor of the Medical Biology Institute, Polish Academy of Sciences.

The project has been carried out in cooperation with the following medical centres: Children's Memorial Health Institute in Warsaw (prof. K. Dzierżanowska-Fangrat), Medical University in Łódź (Perinatology Clinic, Clinic Head: J. Kalinka MD PhD), Collegium Medicum at the Jagiellonian University in Krakow (prof. M. Kosz-Vnenchak and B. Zawilińska MD PhD) and the Polish Mother's Memorial Hospital Research Institute in Łódź.

The cytomegalovirus (HCMV) is found worldwide, with most of the infected population getting it in childhood. Non-specific HCMV antibodies are detected in 70-76% of pregnant women in the Polish population. HCMV is the most frequent cause of intrauterine infections and the most frequent pathogen causing central nervous system diseases and hearing loss in children.

The hypothesis assumes that the antigenic drift in genes encoding other glycoproteins of the coat may affect HCMV virulence and pathogenicity. The overall objective of the Project is to create scientific background related to molecular mechanisms of congenital and postnatal HCMV infections. Studies aimed at identifying the viral and host factors involved in HCMV infection, processes and mechanisms at the interface between the pathogen and the host and at determining the biomarkers of congenital HCMV infections have been scheduled. The study outcomes are expected to provide information on the antigenic drift of viral structures, relationship between the virus genotype and pathogenicity, as well as on the intracellular signal peptides and transcription factors which enable to induce the antiviral response. The following task is carried out within this cooperation: ***Genetic Host Polymorphism Related to the Congenital Immunity Factors versus HCMV Infection (Study of Selected Cytokine and Receptor Expression in term***

Placentas, Mothers and Umbilical Blood)) and whenever any clinical specimens are available from the pregnant women and newborns - the task called**.** ***Detection and Genotyping of Clinical Strains/Isolats from Congenital and Postnatal HCMV Infections*****.**

XII. Grant of the National Science Centre PRELUDIUM9 No. 2015/17/N/NZ6/02015 entitled "RIG-I-like Receptors and the Infection with Human Cytomegalovirus in the Placenta: too much good?". 2016 - 2018**.**

Scientific cooperation: Jarosław Kalinka MD PhD
Project director: mgr Agnieszka Jabłońska. Study supervisor: Edyta Paradowska PhD

The project is aimed at identifying the RIG-I-like receptor (RLR), involved in the recognition of human cytomegalovirus (HCMV) dsRNA and activation of the congenital antiviral response in the human placenta of the third trimester of pregnancy. Particular stress in the studies is put on the identification of factors reducing intrauterine HCMV transmission from the mother's to the fetus's organism.

XIII. A Probe and a Device for Transvaginal Continuous ECG monitoring of the fetus. Perinatology Clinic, MU in Łódź, since 2014

Principal investigator dr med. Michał Skoczylas (Perinatology Clinic at the MU in Łódź), **co-investigators: Jarosław Kalinka MD PhD;** dr inz. Janusz Wróbel (Institute of Medical Technology and Equipment ITAM in Zabrze).

The study is aimed (consent of the Bioethics Committee of the Medical University in Łódź no. RNN/190/15/KE) at the development and clinical verification of the activity of the unique probe and the device for continuous ECG monitoring of the fetus (patent application). In the proposed clinical studies KOMPOREL System will be used for recording and ongoing analysis of signals recorded using a modified pessary. There are plans to use a bioelectrical recording system FETEG, included, to connect the patient. In this way it will be possible to record four signals from measurement electrodes on the pessary perimeter simultaneously.

OTHER STUDY PROJECTS

XIV. Study Title: A phase 2, double-blind, parallel group, randomised, placebo controlled, proof of concept study to assess the safety and efficacy of OBE001 after oral administration in pregnant women with threatened preterm labour.

since 2015

International study, principal investigator: Jarosław Kalinka MD PhD, Perinatology Clinic;

This is a 2nd phase of an international double-blind, multi-center randomised, clinical study, led by ObsEva (Switzerland), assessing the efficiency of an oral tocolytic OBE001 to treat threatened preterm delivery between 34 0/7 a 35 6/7 week of pregnancy when compared to a placebo. OBE001 is a new medication, administered orally. It is an oxytocin receptor antagonist, taken once a day for 7 days.

The major objective of the study is to assess the frequency of deliveries within 7 days after the drug administration. The detailed objectives are the determination of delivery frequency within 48 hours and before 37th week of pregnancy, as well as the morbidity of newborns. The phase 1 clinical studies carried out among non-pregnant women have already been completed and they prove the drug is safe in this group of patients. The study comprises pregnant women with one fetus from 34 0/7 to 35 6/7 week of pregnancy, with threatened preterm delivery, cervix < 25 mm and a positive result of the fibronectin test in the cervicovaginal fluid (> 50 ng/mL).

XV. ZINN (GSK 200721). Randomized , double-blinded, multicenter III phase study comparing efficacy and safety of Retosiban vs Atosiban among women with spontaneous preterm labour and ARIOS - Follow - Up Study to Assess Long-Term Safety and Outcomes in Infants and Children Born to Mothers Participating in Retosiban Treatment Studies.

International study, principal investigator: Jarosław Kalinka MD PhD

Department of Perinatology, Medical University of Lodz , since 2017 - .

1. PB 654 /P05/97/12 - **"Environmental Exposure to Tobacco Smoke and the Health of the Fetus and Newborn"** 01.06.1997-31.12.1998 – **major contractor II- dr Jarosław Kalinka**. Grant director: dr Wojciech Hanke

2. PB PO5D09714 - **"Bacterial and Non-bacterial Risk Factors of Incorrect Pregnancy Course and Outcome"** 1998-2001, grant director: dr Małgorzata Wasiela; **major contractor I - dr Jarosław Kalinka**

3. PB 0567/P05/2003/25 – **"Assessment of the Programme to Counteract Adverse Health-related Effects of Smoking by Pregnant Women"** – 07.10.2003 - 06.10.2004

4. The project commissioned by the Ministry of Science and Higher Education no. PBZ-MeiN-8/2/2006 p.t. **"Epidemiology of Reproductive Threats in Poland - Multicenter, Prospective Cohort Study"** (agreement no. K 140/P01/2007/1.3.1.2). Study task no.: 1.3.1.2 "**Assessment of the Selected Cytokine Concentration in Cervicovaginal Fluid of Pregnant Women as an Early Risk Indicator of Pregnancy Pathology**". **Study task director: Jarosław Kalinka MD PhD;** Perinatology Clinic, MU in Łódź; contractors: prof. Tadeusz Laudański, Perinatology Clinic, MU in Łódź; and prof. Ewa Brzezińska-Błaszczyk, Experimental Immunology Unit, MU in Łódź. **Study director: Jarosław Kalinka MD PhD,** Project director: prof. Wojciech Hanke 2007-2009

5. **"Epidemiology of Reproductive Threats in Poland - Multicenter, Prospective Cohort Study"** Project commissioned by the Ministry of Science and Higher Education, registration no. PBZ-MeiN-8/2**/2006** (agreement no. K 140/P01/2007/1.3.1.2)

   Task 1.3.1.2 "**Assessment of the Selected Cytokine Concentration in Cervicovaginal Fluid of Pregnant Women as an Early Risk Indicator of Pregnancy Pathology**".
   Study task director: Jarosław Kalinka MD PhD
   Project Director: prof. Wojciech Hanke 2007-2009

6. "**Influence of Environmental Pollution and the Socio-occupational Properties of Mothers on the Risk of Preterm Delivery and Fetal Malnutrition"** – subject carried out by the Occupational Medicine Institute and the Institute of Gynecology and Obstetrics of the Medical University in Łódź, subject no.: IMP

10.5, director: dr Wojciech Hanke, main contractors: prof. Wacław Dec and **Jarosław Kalinka MD** 1996-1998

7. "**Assessment of Fetal Malnutrition Treatment Efficiency with Low Doses of Acetylsalicylic Acid"** 1997-1998 – carried out in the Department of Perinatology of the Institute of Gynecology and Obstetrics; **project director –Jarosław Kalinka MD**

8. "**Tobacco Active and Passive Smoking by Pregnant Women, Influence on Low Birth Weight Indexes in the Region of Łódź**", subject no.: IMP 10.9, **main contractor**: Wojciech Hanke MD , **Jarosław Kalinka MD** -1998

9. "**Environmental Support for Pregnant Women who Quit Smoking - Pilot Study**" within the Health and Socio-economic Policy Programme, aimed at reduced tobacco consumption in Poland, project director: Wojciech Hanke MD PhD 1999-2001; **contractor: Jarosław Kalinka MD**

10. "**Threats to the Pregnancy Course and Outcome Related to Working in Farms in the Voivodeship of Łódź**", subject no.: IMP 10.9, main contractor: dr Wojciech Hanke, 1999-2000; **contractor Jarosław Kalinka MD**

11. "**Exposure to Pesticides in Orchards versus Pregnancy Course and Outcome**" IMP 10.9, Wojciech Hanke MD PhD, 2001; **Jarosław Kalinka MD**

12. "**Women's Labour Conditions versus Pregnancy Course and Outcome - Following the Legislation Amendment**" (epidemiological studies), SPR 04.10.49, project director: prof. Teresa Makowiec-Dąbrowska, 01.07.1998 – 31.05.2001; **contractor Jarosław Kalinka MD**

13. **"New Indexes of Biophysical Assessment of Malnourished Fetus Condition during Pregnancy and Labour -** own work at the Medical University in Łódź: 2003-2005, no. 502-11-027: subject director: Michal Skoczylas MD, **contractor Jarosław Kalinka MD**

14. "**Assessment of Proinflammatory Cytokine Level in Vaginal Fluid of Pregnant Women as the Early Marker of Preterm Delivery**" – own work at the Medical University in Łódź: 2001-2003, no. 502-11-735(118): **subject director: Jarosław Kalinka MD**

15. **"Assessment of the Progesterone, Estradiol, PIBF (Progesterone-induced Blocking Factor) and Selected Cytokines in blood serum of women with Threatened Miscarriage, Treated with Dydrogesterone and of women with the Correct Progress of Early Pregnancy"**- the subject performed in the Department of Perinatology, Medical University of Lodz from 2002 to 2008, **study director: J. Kalinka MD**; cooperation: Professor Julia Szekeres-Bartho of the Department of Medical Microbiology and Immunology, Pecs University, Medical School, Hungary and Reproductive and Tumor Immunology Research Group of the Hungarian Academy of Sciences

16. **"Assessment of the Relationship between the Polymorphism of Genes Encoding Selected Proinflammatory Cytokines and the Preterm Labour" -** own work at the Medical University in Łódź: 2005-2007, no. 502-11-363; **study subject**: **Jarosław Kalinka MD PhD**

17. **"Prevention of Incorrect Uterus Contraction and Bleeding following Cesarian Cut with Carbetocin (Pabal)"** The project was carried out in the Department of Perinatology at the Medical University in Łódź. 2007-2012**. Study director: Jarosław Kalinka MD PhD**

18. **Assessment of the Immune System Cell Activity Changes in Endometrium during a Physiological Menstrual Cycle, in Decidua in Physiological Conditions and in Pathological Conditions Complicating Pregnancy and in the Endometriosis Centres and in Ovarian Tumour" No. 0888/B/P01/2008/35**
Director prof A. Basta, Clicni of Gynecology and Oncology, Collegium Medicum at the Jagiellonian University**; Contractor Jarosław Kalinka, MD PhD Department of Perinatology, the Medical University in Łódź**

19. **"Assessment of the Molecular Mechanisms at the Interface between a Human Body, Pathogens and Environmental Factors (InterMolMed)". Task 2, called "Identification of Molecular Mechanisms of Viral Infections and Non-specific Congenital Immunity, as well as New Therapeutic Shields and Anti-viral Agents. Medical Experiment within the Research Project of the Innovative Economy Programme no. POIG.01.01.02-10-107/09." 2010-2014**
Scientific cooperation: Jarosław Kalinka MD PhD
Task 2 Director: prof. Zbigniew J. Leśniewski, Medical
Biology Institute, Polish Academy of Sciences

20. **Grant of the National Science Centre OPUS7 No. 2014/13/B/NZ7/02317 called. "Risk Factors for Congential and Postnatal Infections with Cytomegalovirus". 2015-2018.**
Performed by: **Jarosław Kalinka MD PhD**
Project director: Edyta Paradowska PhD, Professor of the Medical Biology Institute, Polish Academy of Sciences.

21. **Grant of the National Science Centre PRELUDIUM9 No. 2015/17/N/NZ6/02015 entitled "RIG-I-like Receptors and the Infection with Human Cytomegalovirus in the Placenta: too much good?". 2016-2018.**
Scientific cooperation: Jarosław Kalinka MD PhD
Project director: mgr Agnieszka Jabłońska.

22. **Assessment of the Association between Vitamin D Concentration in the Blood Serum of Parturients and the Pregnancy Duration, Including the Effect of Selected Genetic Factors"**

Grant of the National Science Centre - Preludium 4

Number: UMO-2012/07/N/NZ5/01720 2013-2016

Patron/Advisor: Jarosław Kalinka MD PhD

Project director: physician Marta Baczyńska-Strzecha

23. **Study Title: A phase 2, double-blind, parallel group, randomised, placebo controlled, proof of concept study to assess the safety and efficacy of OBE001 after oral administration in pregnant women with threatened preterm labour.**
International study, principal investigator: Jarosław Kalinka, MD PhD
Department of Perinatology, Medical University of Lodz, since 2015.

24. **ZINN (GSK 200721). Randomized , double-blinded, multicenter III phase study comparing efficacy and safety of Retosiban vs Atosiban among women with spontaneous preterm labour and ARIOS - Follow - Up Study to Assess Long-Term Safety and Outcomes in Infants and Children Born to Mothers Participating in Retosiban Treatment Studies.**

International study, principal investigator: Jarosław Kalinka, MD PhD

Department of Perinatology, Medical University of Lodz , since 2017.

Grants funded by the European Union

23. PHARE grant "***The Effect of Environmental and Socio-occupational Characteristics of Mothers on the Risk of Small-for-gestational-age (SGA) Babies and Preterm Deliveries.*** 1996. - Grant from the Foundation for Polish Science to design study programmes of the European Union, funded by SCI-TECH Phare, with respect to identifying the risk factors of fetal malnutrition and preterm delivery (with W. Hanke MD), completed on 31.12.1997.

Teaching

From the very beginning of my employment at the Medical University in Łódź I have been an active lecturer in the Department of Perinatology, 1 Chair of Gynecology and Obstetrics at the Medical University in Łódź. I have taught classes and seminars devoted to obstetrics and gynecology for 5th- and 6th-year students of the Faculty of Medicine.

I have taught seminars and practical classes for 5th-year students of the Dentistry Faculty and students of the Public Health Faculty and the Emergency Medicine Faculty. I have also given lectures to ^{4th}-, 5th and 6th-year students of the Medical Faculty (sample lecture subjects: "Physiological labour", "Preterm delivery", "Premature rupture of membranes" or "Forceps procedure".

I have also carried out practical and theoretical examinations in gynecology and obstetrics for 6th-year students of the Medical Faculty.

I was an advisor of the Emergency Medicine students at the MU with respect to gynecology and obstetrics classes.

I have participated also in courses preparing for specialising in gynecology and obstetrics (e.g.: "Sexually transmitted diseases (STD)", "Preterm delivery") and in postgraduate training for physicians, courses preparing for specialising in gynecology and obstetrics, as well as for the listeners of the "Health Promotion" course.

I have given lectures and been a member of the Jury assessing scientific works of students at the Conference of Students Gynecological Associations "***The Latest Trends in Gynecology, Obstetrics, Perinatology and Uroginecology"*** held under the auspices of the Polish Gynecological Society (PGS) in 2014. The students' works prepared in the Perinatology Clinic of the Medical University in Łódź, presented at

the said Conference, were awarded. The results of the scientific work with the students of the MU in Łódź were published in ***MedGinProject. 2014****, 4 (34): 61-71 ("Sleep Disorders of Pregnant Women) and* ***MedGinProject. 2015****; 1 (35): 43-52 ("Assessment of the Sleep Apnea Risk in the Third Trimester of Pregnancy"*).

I was also an individual scholarly advisor of 4th and 5th-year student of the Medical Faculty (Individual Education Programme).

I have given numerous lectures at the Polish and foreign conferences and scholarly meetings, as well as invited by regional branches of **the Polish Gynecological Society (PGS) and the Polish Perinatal Medicine Society (PTMP**).

The sample lecture subjects included:

- **Kalinka J:** The role of the immunological factors in early pregnancy failure and in preterm delivery. International Workshop on Air Pollution and Human Reproduction. GSF-National Research Center for Environment and Health, Institute of Epidemiology. Munich, Germany 08-11.05.2007
- **Kalinka J:** Progesterone in prevention of preterm labour. International Congress in Fetal Medicine. Warsaw, Poland 8-10 September 2008
- **Kalinka J:** Genetyczne uwarunkowania porodu przedwczesnego. Ciąża wysokiego ryzyka [Genetic Predispositions to Preterm Delivery. 5th Congress of the Polish Society of Perinatal Medicine "Perinatology in 21st Century" Łódź, 25-27 June 2009:
- **Kalinka J:** Przedwczesne pęknięcie błon płodowych – ciągle aktualny problem medycyny perinatalnej. [Premature Rupture of Membranes - A Still Current Problem of the Perinatal Medicine. Abstracts from XXXI Congress of the Polish Ginecological Society, Katowice 19-22 September 2012.
- **Kalinka J:** The impact of fetal carriage of TLR4 gene polymorphisms (896A>G, 1196C>T) on the risk of prematurity in the Polish population – preliminary report. XXIV European Congress of Perinatal Medicine, Florence, Italy, June 4th-7th 2014
- **Kalinka J:** Najczęstsze błędy w decyzji o cięciu cesarskim. [The Most Frequent Errors of Decisions on Cesarean Cuts]. IX Congress of Akademia po Dyplomie. Warsaw, 24-25 April 2015
- **Kalinka J:** Poród przedwczesny – krótka szyjka macicy – aktualne strategie postepowania. [Preterm delivery - short cervix - current procedure] XXXII Congress of the Polish Gynecological Society. Łódź, 3-5 September 2015.

I am a coauthor of **8 chapters** in handbooks for physicians and students, devoted to the aspects of obstetrics and perinatology (including: "Late premature newborns", "Environmental and occupational risk factors of preterm delivery", "Genetic predispositions to preterm delivery", "Progesterone in preterm delivery prevention" or "Incorrect pregnancy duration: Preterm Delivery. Prolonged pregnancy"), in such handbooks as: "*Ciąża wysokiego ryzyka*" [*High-risk Pregnancy*], "*Położnictwo tom 2*"

[*Obstetrics vol.2*] , "*Medycyna matczyno-płodowa*" [*Maternal and Fetal Medicine*], "*Położnictwo i Ginekologia, Tom 1*" [*Obstetrics and Gynecology, vol. 1*] or "*Sytuacje kliniczne w położnictwie*" [*Clinical Situations in Obstetrics*]. Nowadays, those are the basic handbooks for students and physicians preparing for the specialisation exam in obstetrics and gynecology, as well as in perinatology.

In 2009, I was appointed a member of the Team for Scholarly Scores at the Medical University in Łódź for one term of office by the President and the Senate Committee for Science.

In 2010, I was appointed a consultant in the Senate Committee for the Construction of the Clinical & Teaching Centre of the MU in Łódź in the field of gynecology and obstetrics.

Since 2006, I have been a member of the Medical Faculty Council of the Medical University in Łódź and a member of the Scientific Council of 1st Chair of Gynecology and Obstetrics at the MU in Łódź.

In years: 2008-2011 I was a member of Prof. dr med. Jerzy Nofer Scientific Council of the Occupational Medicine Institute in Łódź.

I was an advisor of two doctoral students with respect to medical sciences (1. physician Marcin Serafin: "***Wpływ polimorfizmu wybranych loci genów kodujących cytokiny: IL-1β, IL1RA, IL-6 I TNFα u kobiet ciężarnych na ryzyko wystąpienia porodu przedwczesnego w populacji polskiej***" [Influence of the Polymorphism of Selected Loci of Cytokine-encoding Genes: L-1β, IL1RA, IL-6 I TNFα in Pregnant Women on the Risk of Preterm Delivery in the Polish Population] - Defended on: 08.01.2014 at the MU in Łódź and 2. physician Maria Prośniewska-Obsada: "**Ocena nosicielstwa paciorkowców grupy B (GBS) wśród kobiet ciężarnych oraz określenie medycznych, demograficznych i mikrobiologicznych czynników ryzyka nosicielstwa GBS u matek i infekcji wrodzonych u noworodków**" [Assessment of the B-group streptococcus (GBS) in Pregnant Women and Determination of Medical, Demographic and Microbiological Risk Factors of GBS Presence in Mothers, as well as Congenital Infections of Newborns] - Defended 22.10.2014, at the MU in Łódź

At present, I have supervised two doctoral students, who have had their doctoral dissertation reviewed and accepted:

- physician Maria Baczyńska: "*Ocena związku pomiędzy stężeniem witaminy D w surowicy krwi kobiet rodzących, a długością trwania ciąży i urodzeniowa masą ciała noworodków*" [Assessment of the Relationship between Vitamin D Concentration in the Blood Serum of Parturients, and the Pregnancy Duration and the Newborn Body Weight] – open 28.05.2012 MU in Łódź, expected completion: June 2017, and

- physician Tomasz Jarzębski: "*Związek stężenia witaminy D z wybranymi patogenami bakteriologicznymi oraz czynnikami immunologicznymi u kobiet rodzących, z uwzględnieniem samoistnego porodu przedwczesnego*" [Relationship between Vitamin D Concentration and Selected Bacteriological Pathogens and Immune Factors in Parturients, including Spontaneous Preterm Delivery], open: 19.05.2014 MU in Łódź, expected completion: 2017.

I also reviewed 5 PhD theses, defended e.g. at the Medical Faculty of the Warsaw Medical University, Medical Faculty of the Medical University in Białystok, Collegium Medicum of the Jagiellonian University in Krakow and at the Faculty of Health Sciences at the Pomeranian Medical University in Szczecin.

Moreover, I was an advisor of 2 MA theses at the Faculty of Health Sciences, Department of Nursing and Midwifery, majoring in Midwifery at MU in Łódź and a reviewer of 1 MA thesis.
I was also a supervisor/advisor of the scientific grant from the National Science Centre within PRELUDIUM 4 programme. The project director: physician Marta Baczyńska-Strzecha won an award for the said work in the competition for scholars below 34 years of age by the ***International Society of Gynecological Endocrinology (ISGE***) in 2016.
I was a director of 4 specialisations in the field of gynecology and obstetrics, and now I am a director of 1 specialisation in perinatology.

Organisational activities

Since 2007, I have been an active member of the international group called **PREBIC (*Preterm Birth International Collaborative*) and PREGENIA**. I have participated in annual meetings of both scientific societies, held by the Department of Reproductive Health and Research World Health Organization; **WHO Headquarters, Geneva and March of Dimes, USA** in Geneva, Switzerland.

In 2011 I organised the **first international scientific meeting of the PREBIC group: *1st International Satellite PREBIC Meeting* in Łódź**, Poland, devoted to broadly-taken aspects of preterm delivery.

My international activity brought me an invitation to the **Advisory Board of "*2nd European Spontaneus Preterm Birth Congress*"**, held on 26-28 of May 2016 in Göteborg, Sweden, and organised by FIGO and the March of Dimes.

Active participation in the Conference of Students Gynecological Associations, held under the auspices of the Polish Gynecological Society, "***The Latest Trends in Gynecology, Obstetrics, Perinatology and Uroginecology***" taking place from 29 to

30.03.2014 in the Teaching Centre of the Medical University in Łódź (jury, lectures). The results of the scientific work with the students of the MU in Łódź were published in ***MedGinProject. 2014, 4 (34): 61-71 ("Sleep Disorders of Pregnant Women) and MedGinProject. 2015; 1 (35): 43-52 ("Assessment of the Sleep Apnea Risk in the Third Trimester of Pregnancy").***

I was the main organiser of and gave lectures during the so-called "Open days of M. Pirogow (formerly M. Madurowicz) Hospital", under the auspices of the Łódź Branch of the Voivodeship National Health Fund (NFZ) and the MU in Łódź from 7 to 12 of March 2016. The meeting participants had a chance to listen to specialist speeches (by physicians, midwives, psychologists and physiotherapists) concerning e.g. the current care standards for pregnant women, course of pregnancy, labour, as well as the correct care of the mother and child in the first weeks of life. Moreover, I gave lectures for secondary school students, to get them acquainted with the aspects of pregnancy physiology and modern contraceptives. On a regular basis, I have given press, radio and TV interviews on the general care of women with gynecological and obstetric problems, paying particular attention to problems related to pregnancy and labour.

Clinical activity

Since July 2008 until today **I have been a Head of the Perinatology Ward and the Labour Ward**in the **M. Pirogow (formerly M. Madurowicz) Voivodeship Specialist Hospital.** This is a Surgical Department with 56 beds, composed of the Labour Ward, Prepartum Ward and Postpartum Ward, as well as the operating theatre. **The Department has the highest, 3rd reference degree of the perinatal care** (one of two such centres in the region of Łódź). This Department treats pregnant women and parturients belonging to high risk group. When managing the Department, I developed modern diagnostic, therapeutic and surgical standards and introduced them to the clinical practice, including with respect to peripartum bleeding, preterm deliveries and peripartum supervision techniques. The introduced organisational changes helped to reduce the morbidity and mortality rate of parturients and their newborns.

Awards:

2007 **First degree, individual, scholarly award of the University President for the habilitation thesis** called "**Assessment of Selected Risk Factors of Limited Fetal Growth and Preterm Delivery, Using Biological Indexes and Biomarkers of Exposure**", Medical University in Łódź

2006 **Second degree, individual, award of the University President for scientific activity in 2005, Medical University in Łódź**

2005 **Kalinka J, Hanke W, Sobala W: "***Impact of Prenatal Tobacco Smoke exposure, as Measured by Midgestation Serum Cotinine Levels, on Fetal Biometry and Umbilical Blood Flow Velocity Waveforms***." American Journal of Perinatology 2005, 22: 41-47; The work obtained distinctions for publication in 2006 Year Book of Obstetrics, Gynecology and Women' Health; Mosby Publishing House, Elsevier Health Science, U.S.**

2003 **International Cytokine Society Award: The Frederica Fischer Foundation Fellowship, Dublin, Ireland**

1999 **IV World Congress of Perinatal Medicine, Buenos Aires, Argentina: Poster Award, Mention of Honor**

1999 **Conference called "Challenges to Epidemiology in changing Europe", Krakow, Poster of Distinction**

I was also a supervisor/advisor of the scientific grant from the National Science Centre within PRELUDIUM 4 programme. The project director: physician Marta Baczyńska-Strzecha won an award for the said work in the competition for scholars below 34 years of age by the ***International Society of Gynecological Endocrinology (ISGE*) in 2016.**

Moreover, the works by students prepared in the Perinatology Clinic at the Medical University in Łódź were awarded at the Conference of Students Gynecological Associations called "***The Latest Trends in Gynecology, Obstetrics, Perinatology and Uroginecology",*** held under the auspices of the Polish Gynecological Society (PGS) in 2014 (**recognised in the oral session devoted to Obstetrics).**

I was also awarded two rewards of: "**Personality of Year 2014** of the **Area of Łódź" in the category of medicine** (Łódź 2014) and "**Personality of Year 2015 in the category of medicine" (Warsaw 2015**) by "Osobowości i sukcesy" magazine.

Membership

Since 2007, I have been a member of the international **PREBIC (Preterm Birth International Collaborative**) group with its seat in Geneva (Switzerland, by 2016) and currently in Galveston, Texas, U.S., the meetings of which are held under the patronage of WHO and the March of Dimes from the U.S. I have also been a member of

PREGENIA (**Preterm Birth and Genetics International Alliance**), **U.S.** and ***Preterm Birth Genome Project Consortium, U.S.*** cooperating with the PREBIC group.

Nowadays (since 2015) I have been a **President-Elect of the Polish Society of Perinatal Medicine (PTMP)** and a member of the **Management Board of the Perinatology Division of the Polish Society of Perinatal Medicine (PTG).** In 2015 I became a member of the **Management Board of the Łódź Branch of the Polish Gynecological Society.**

For three terms, I have also been a member of the Management Board of the Polish Society of Perinatal Medicine (PTMP).

I am also a member of the ICM Research Advisory Network, United Kingdom, the European Association of Perinatal Medicine and a Member of Global Obstetric Network – GoNet.

I have been a member of editorial committees and scientific councils of the following journals:

- **Editorial Board BMC Pregnancy and Childbirth, BioMed Central Ltd, London, United Kingdom**
- **Scientific Council of "Ginekologia po Dyplomie**"
- **Member of Editorial Board: Archives of Perinatal Medicine.**

I was appointed a reviewer of the National Science Centre to assess the scientific conclusions.

I was a member of the **Expert Teams of the Polish Gynecological Society (PGS):**

- twice in 2012 and 2013. The opinion of the Expert Team of the Polish Gynecological Society with Respect to Carbetocin Administration to Prevent Postpartum Bleeding (*1.Poręba R, Oszukowski P, Oleszczuk J, Bręborowicz G, Wielgoś M, Czajkowski K, Smolarczyk R, **Kalinka J**: Opinion of the Expert Team of the Polish Gynecological Society concerning Carbetocin Administration to Prevent Postpartum Bleeding - Knowledge as at 2012. Ginekologia i Położnictwo Medical Project. 2012, 2: 56-58 and 2. Poręba R, Oszukowski P, Oleszczuk J, Bręborowicz G, Wielgoś M, Czajkowski K, Smolarczyk R, **Kalinka J:** Extended opinion of the Expert Team of the Polish Gynecological Society concerning Carbetocin Administration to Prevent Postpartum Bleeding. Ginekologia i Położnictwo Medical Project 2013;1(27): 41*) and
- in 2016 The opinion of the Expert Team of the Polish Gynecological Society concerning preventive administration of folic acid and metafolin.

Moreover, I participated in preparing "*The Interdisciplinary Procedure in Obstetric Bleeding - Consensus of An Anesthesiologist and Obstetrician A.D. 2016. 1st Educational*

Conference "Bleeding in Gynecology in Practiced, Based on Clinical Cases A.D. 2016", Warsaw 2016

I participated actively in the international meeting of the expert team, devoted to the preventive carbetocin administration aspects to prevent peripartum bleeding in women giving birth vaginally - Paris, 2013.