Description of scientific record and research achievement

PhD in medical biology
Elżbieta Gałecka

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Łódź 2018

1. First name and family name

Elżbieta Anna Gałecka

2. Diplomas and academic degrees

19/05/1999	Master of Science in Pharmacy Faculty of Pharmacy of the Medical University of Lodz, Poland
2000	Right to exercise the profession of pharmacist District Pharmaceutical Chamber in Lodz, Poland
9/04/2003	First degree specialist in retail pharmacy
24/06/2008	PhD in medical sciences, medical biology, biochemistry specialisation; doctoral thesis entitled: "Effects of serotonin reuptake inhibitor and nonsteroidal anti-inflammatory drug on oxidative and reductive processes in patients with depressive disorders" (supervisor: Professor Józef Kędziora, PhD), Faculty of Military Medicine, Medical University of Lodz

3. Information on current employment in research and scientific institutions

06/01/2006 – 31/01/2008	Assistant, Clinical Chemistry and Biochemistry Unit, Department of Clinical Chemistry and Biochemistry, Faculty of Military Medicine, Medical University of Lodz
1/08/2008 – 31/07/2013	Assistant Professor, Molecular Endocrinology Laboratory, Institute of Endocrinology and Metabolic Diseases, Department of Endocrinology and Metabolic Diseases, Medical University of Lodz
2013 – present	Specialist for scientific and technical matters, Institute of Pneumonology and Allergology, 1st Department of Internal Medicine, Medical University of Lodz

4. Scientific achievement under Article 16(2) of the Act of 14 March 2003 on Academic Degrees and Academic Title and Degrees and Title in Art (Official Journal of the Republic of Poland No. 65, item 595, as amended):

(a) research achievement title:

Research on the role of genes and expression of iodothyronine deiodinases in recurrent depressive disorders

The research covering the scope of the scientific achievement constitutes a cycle of 5 original publications.

(b) Author(s), title(s) of publication, year of publication, volume, page numbers:

1. Gałecka E, Talarowska M, Orzechowska A, Górski P, Bieńkiewicz M, Szemraj J. Association of the DIO2 gene single nucleotide polymorphisms with recurrent depressive disorder. Acta Biochimica Polonica 2015;62: 297-302.
(IF 1.187; Ministry of Science and Higher Education 15)

2. Gałecka E, Talarowska M, Orzechowska A, Górski P, Szemraj J. Polymorphisms in the type I deiodinase gene and frontal function in recurrent depressive disorder. Advances in Medical Science 2016; 61: 198-202.
(IF 1.364; Ministry of Science and Higher Education 15)

3. Gałecka E, Talarowska M, Maes M, Su KP, Górski P, Szemraj J. Polymorphisms of iodothyronine deiodinases (DIO1, DIO3) genes are not associated with recurrent depressive disorder. Pharmacological Reports 2016; 68: 913-7.
(IF 2.587; Ministry of Science and Higher Education 25)

4. Gałecka E, Kumor-Kisielewska A, Orzechowska A, Maes M, Górski P, Szemraj J. Assessment of type 1 and type 3 deiodinase expression levels in depressive disorders. Acta Neurobiol Exp (Wars). 2017;77: 225-235.
(IF 1.5; Ministry of Science and Higher Education 20)

5. Gałecka E, Talarowska M, Su KP, Górski P, Kumor-Kisielewska A, Szemraj J. Expression levels of interferon-γ and type 2 deiodinase in patients diagnosed with recurrent depressive disorders. Pharmacological Reports 2018; 70:133-138.
(IF 2.787; Ministry of Science and Higher Education 25)

Total Impact Factor for the papers reported as achievement – 9,425
Score according to the Ministry of Science and Higher Education – 100

(c) Description of the main aim of above mentioned studies, their results and potential use.

The presented work cycle concerns unipolar depression in the course of recurrent depressive disorders (RDD). The relationships between *DIO1, DIO2, DIO3* genes and their expression and RDD were evaluated. The publications in the postdoctoral cycle are the result

of work conducted within the framework of the Opus 4 grant, financed by the National Science Centre, entitled "Iodothyronine deiodinase encoding genes, expression at mRNA and protein levels in the complex mechanism of recurrent depressive disorders" 2012/07/B/NZ7/04212, 05.07.2018 – 04.07.2016. The research was carried out in cooperation with the Department of Adult Psychiatry and the Department of Medical Biochemistry of the Medical University of Lodz.

One of the most common and diagnosed mental illnesses in Poland and worldwide are recurrent depressive disorders. It is estimated that by 2020 it will be the third or the second most commonly diagnosed disease entity [Gilman et al., 2017]. It is a disease entity of heterogeneous aetiology. Despite intensive research, all the direct factors causing the disease are not known. It is necessary to search for them because, according to the World Health Organization, depression will be the second disease entity causing disability in terms of the number of affected people. Psychological, environmental and genetic factors are considered predisposing factors [Lopizzo et al., 2015; Rottenberg et al., 2015]. Among various hypotheses of depression development, the new neurodevelopmental theory is of particular interest [Gałecki and Talarowska, 2018].

Recurrent depressive disorders occur as a single disease entity. Their coexistence with other diseases and the development of depression as a result of somatic diseases are characteristic [Maier and Falkai, 1999]. The coexistence of depression in the course of thyroid diseases and disorders is observed; additionally, disorders of the hypothalamic–pituitary–thyroid axis are characteristic of depression [Bauer et al., 2009]. For example, an elevated concentrations of TRH in cerebrospinal fluid are observed, along with decreased expression of mRNA for THR, elevated levels of thyroxine (T4) [Baumgartner et al. 1988] and reverse triiodothyronine (rT3) in cerebrospinal fluid [Linnoila et al., 1982]. Animal model studies report an increase in the concentration of triiodothyronine (T3) in the brain after treatment with antidepressants such as paroxetine, venlafaxine, and tianeptine [Pina et al., 2003]. There are reports of significant effects of thyroid hormones on mood and behaviour [Mazza et al., 2008]. Thyroid disorders may lead to the manifestation of certain features observed in depression. For example, attention, concentration, memory and psychomotor dysfunctions occur in hypothyroidism [Bauer, 2008, Samuels, 2008; Bonnin et al., 2010]. The therapeutic efficacy of triiodothyronine (T3), as a supplement to antidepressant therapy, has been observed. There is evidence of the antidepressant effect of high doses of T3 and T4. Studies on animals also indicate the effect of various antidepressants on changes in the activity of type 2 and type 3 deiodinases of enzymes involved in the synthesis of thyroid hormones [Ervaci et al., 2000; Baumgartner et al., 1994].

Another process observed in depression is inflammation. For example, there is an increase in the concentration of proinflammatory cytokines and an increase in the number and activity of monocytes, macrophages and other immune cells and molecules [Gałecki et al., 2018].

Three enzymes involved in the synthesis and transformation of thyroid hormones are important determinants of their concentration. These are selenoenzymes: iodothyronine deiodinase type 1 (DIO1), type 2 (DIO2) and type 3 (DIO3). Under normal conditions, the enzyme that generates the main amounts of T3 peripherally is DIO1. Expression of this enzyme is observed in the thyroid gland, kidneys and liver. The enzyme is also expressed in lymphocytes, and one of the factors inducing DIO1 expression includes proinflammatory cytokines. The role of this enzyme as a neuronal source of T3 should be emphasised, where the hormone reaches directly from peripheral blood and cerebrospinal fluid. Another enzyme is DIO2, which also generates T3 concentration peripherally. It is characterised by tissue specificity. DIO2 is expressed, *inter alia*, in the glial cells of the brain, where the concentration of T3 is the result of local conversion of T4 by deiodination. Animal model studies have shown that lack of mRNA expression for DIO2 may result in decreased T3 levels in the brain. The concentration of reverse triiodothyronine (rT3) is determined by DIO3 through reductive inner ring deiodination of T4. DIO3 is also involved in the transformation of T3 to diiodothyronine (T2). DIO3 expression was observed in most organs, including the brain, and especially in neurons of the hippocampus, cerebellum and frontal cortex, i.e. the regions important for depression development [Bernal, 2002]. Under pathological conditions of an inflammatory process, this enzyme is expressed in monocytes and macrophages [Korle, 1999].

Research on the aetiology of depression indicates the importance of genes for the development of the disease. Certain data are available regarding the importance of the expression of molecule-encoding genes associated with the functioning of the hypothalamic–pituitary–thyroid axis in depression. The *SLCO1C1* gene of thyroid hormone transporter is associated with the risk of development of depressive disorders [van der Deure et al., 2005]. Peeters et al. observed a correlation between the polymorphism of the *DIO2* gene and changes in hormone levels in the thyroid gland. A relationship was observed between *DIO2* polymorphism, T3 concentration and enzyme activity [Canani et al., 2005]. Genetic variants (polymorphisms), expression at the mRNA and protein levels of the genes responsible for the synthesis and concentration of thyroid hormones are considered potential genetic risk factors for RDD. Thyroid hormones synthesised by deiodinases are important for normal brain function, especially the limbic system, which has a high number of receptors for thyroid hormones and whose functional changes are important in the pathophysiology of depression [Bauer et al., 2008].

Analysing the available literature, it is worth noting that so far three studies regarding patients with mental disorders have been published, assessing the relationship between the genes encoding deiodinases and the disease and its course. The relationship between the *DIO2* gene and the bipolar affective disorder was evaluated and the dependence between *DIO1* and a response to antidepressant therapy was assessed. Moreover, the influence of DIO1

on depression episodes was analysed [He et al., 2009; Philibert et al., 2011; Cooper-Kazaz et al., 2009].

Main research objectives:

1. To assess whether there is a correlation between the occurrence of single nucleotide polymorphisms of *DIO1, DIO2, DIO3* genes and the risk of RDD development.
2. To estimate the frequency of genotypes and alleles; to assess the risk of falling ill depending on the prevalence of a given genotype or allele, and to assess the relationship between the genetic variant and psychological and clinical features, as well as to assess genotype or allele prevalence variability between patients with diagnosed RDD and a healthy group.
3. To estimate the frequency of *DIO2* Thr92Aa (T/C) and ORFa-Gly3Asp (C/T) haplotypes in the studied populations and to seek the relationship between the risk of RDD and the prevalence of the haplotypes.
4. To evaluate expression of the examined genes in patients with RDD and to perform a comparison with a control group as well as to search for a relationship between expression and clinical features.

The studies were performed in patients diagnosed with RDD on the basis of the criteria for classification of mental and behavioural disorders contained in ICD-10 (F33.0-F33.8) (World Health Organization 1992).

Gałecka E, Talarowska M, Orzechowska A, Górski P, Bieńkiewicz M, Szemraj J. Association of the DIO2 gene single nucleotide polymorphisms with recurrent depressive disorder. Acta Biochimica Polonica 2015;62: 297-302

My contribution to this paper involved working out the concept of research, research planning, performing experiments, analysing the results, reviewing the literature, preparing a manuscript, correcting the paper after review and formulating answers for reviewers. My percentage contribution is estimated at 80%.

The paper begins with a section devoted to the importance of genes encoding iodothyronine deiodinases in RDD. The relationship between single nucleotide polymorphisms: Thr92Ala, ORFa-Gly3Asp of the *DIO2* gene and the risk of RDD development was investigated. There are data on the relationship between genetic variants of *DIO2* and protein concentration, enzymatic activity of DIO2 and thyroid hormone concentration. Earlier studies have shown that the T allele of the Thr92Ala (T/C) variant correlates with both higher DIO2 activity and thyroid hormone concentration, while the C allele of the ORFa-Gly3Asp (C/T) variant correlates with decreased enzyme activity and reduced hormone concentration. The single polymorphism of Thr92Ala (rs225014) is located in nucleotide 674 and is characterised by an exchange of threonine (Thr)T for alanine (Ala)C in codon 92. On the other hand, the

ORFa-Gly3Asp (12885300) polymorphism is a polymorphism in an open reading frame, in the region not subject to translation, and is characterised by the exchange of glycine (Gly)C for asparagine (Asp)T. It was observed that the CC genotype of the Thr92Ala variant was significantly less frequent in the affected patients than in the control group, and was associated with a lower risk of depression (OR=0.09; CI = 0.01-0.82; p = 0.03). A small percentage of its prevalence was confirmed, which was also reported by other researchers. A significant difference was found in the distribution of the analysed haplotypes among the studied groups. The T-C (Thr-Gly) haplotype occurs more often in the patients suffering from depression and is associated with an elevated risk of depression development (OR=1.59; 1.05-2.38; p=0.03). Based on the obtained results the significance of *DIO2* gene as a possible factor for RDD pathological mechanism can be suggested.

Gałecka E, Talarowska M, Orzechowska A, Górski P, Szemraj J. Polymorphisms in the type I deiodinase gene and frontal function in recurrent depressive disorder. Advances in Medical Science 2016; 61: 198-202.

My contribution to this paper involved working out the concept of research, research planning, performing experiments, analysing the results, reviewing the literature, preparing a manuscript, correcting the paper after review and formulating answers for reviewers. My percentage contribution is estimated at 80%.

The paper serves as continuation of the research on the significance of genes for deiodinases in depression and its accompanying dysfunctions. The disorders accompanying RDD include disorders of memory processes, which often correlate with an early onset of depression symptoms and with prolongation of the episode. Among cognitive dysfunctions, the following should be noted, which are particularly dependent on cortical functions: concentration, operating memory, executive functions. Thyroid hormones and the signal transmission processes associated with them, by means of impacting neurogenesis, neurotransmission and gene expression, play an important role in the proper functioning of the brain, especially in those regions that are important for memory processes.

A correlation was observed between a polymorphism of the *DIO1* gene and the concentration of thyroid hormones in the serum. This applies to two functional polymorphisms, i.e. DIO1a-C/T and DIO1b-A/G. According to Peeters et al. [2005], the T allele of the DIO1a-C/T variant correlates with increased rT3 concentration and lower T3/rT3 ratio, while the G allele of the DIO1b-A/G polymorphism correlates with higher T3/rT3 ratio. The aforementioned two functional polymorphisms of the *DIO1* gene were analysed during the study and correlated with cortical memory functions such as: operating memory, executive functions, and verbal fluency.
The evaluation of cognitive processes was carried out using the Trial Making Test, the Stroop test and the verbal fluency test. The obtained genotype frequencies for the studied

polymorphisms were in accordance with the Hardy–Weinberg equilibrium, which confirms the representative nature of the selected group. The prevalence of genotypes and alleles for the polymorphisms studied is similar to that of other authors in the Caucasian population. A significant correlation was found between CT and TT genotypes of the *DIO1a* C/T variant and verbal fluency. No significant differences were observed between the distribution of genotypes or between demographic and clinical parameters.

Gałecka E, Talarowska M, Maes M, Su KP, Górski P, Szemraj J. Polymorphisms of iodothyronine deiodinase (DIO1, DIO3) genes are not associated with recurrent depressive disorder. Pharmacological Reports 2016; 68: 913-7.

My contribution to this paper involved working out the concept of research, research planning, performing experiments, analysing the results, reviewing the literature, preparing a manuscript, correcting the paper after review and formulating answers for reviewers. My percentage contribution is estimated at 80%.

The relationships between genetic variants of *DIO1* and *DIO3* genes and RDD were sought. Genetic variants in the genes related to thyroid hormone metabolism can affect protein expression, enzyme activity and the final result. Where the functionality of a given variant is unknown, it is likely that the polymorphism in question is in "linkage disequilibrium", i.e. the balance of linkage with the functional polymorphism located within the area of the same gene or a gene located in the vicinity. Previous studies have shown the relationship between the DIO1a(C/T) genetic variant and unipolar depression, and between this variant and the efficacy of T3 supplementation of antidepressant therapy. Two polymorphisms of gene *DIO1a*-(C/T), *DIO1b*-(A/G), and *DIO3*-(C/T) and (A/C), were analysed in this study. These polymorphisms, as well as the polymorphisms of the *DIO2* gene presented above, have not been studied in unipolar depression so far. The obtained results did not show any significant correlation between the four polymorphisms and RDD. No interrelation between genotype distribution and demographic and clinical parameters was found. The calculated value of the risk of falling ill did not confirm any genotype or allele as a positive or negative factor of depression development. No previous reports of other researchers on the relationship of genes encoding deiodinases, especially regarding the *DIO1* gene, with unipolar depression were confirmed.

Gałecka E, Kumor-Kisielewska A, Orzechowska A, Maes M, Górski P, Szemraj J. Assessment of type 1 and type 3 deiodinase expression levels in depressive disorders. Acta Neurobiologiae Experimentalis (Wars). 2017;77: 225-235.

My contribution to this paper involved working out the concept of research, research planning, performing experiments, analysing the results, performing a statistical analysis,

reviewing the literature, preparing a manuscript, correcting the paper after review and formulating answers for reviewers. My percentage contribution is estimated at 80%.

Changes in thyroid hormone concentration and inflammatory process participate in the complex mechanism of depression development during RDD. There are data on the interactions between interleukins and deiodinases and the contribution of these molecules to immunological processes. According to the available literature, certain studies evaluated the expression of deiodinases. So far, no attempt has been made to assess the expression of DIO1 and DIO3 in patients with diagnosed depression. In the case of depression, it may be particularly important to evaluate the expression of DIO1 and DIO3 genes in brain cells; however, according to Metha et al., the processes observed on the periphery may reflect those occurring in the central nervous system. The importance of a peripheral inflammatory process in the aetiology of depression should also be emphasised.

The results of the studies showed the expression of type 1 and type 3 deiodinases in both the affected patients and the control group. Similarly, the expression of the *DIO1* gene was observed by Nishikawa et al. in mononuclear cells of peripheral blood in patients suffering from the Graves' disease. In our study we found a significantly lower level of both DIO1 expression and protein concentration in the affected patients than in the control group. This partially explains the decreased concentration of T3 in the patients with depression or the development of depressive disorders in the case of hypothyroidism or other dysfunctions of the hypothalamic–pituitary–thyroid axis. In turn, DIO3 expression was higher in the affected patients than in the control group. Considering the contribution of DIO3 to the course of immune and inflammatory processes, increased expression of DIO3 may indicate the importance of this molecule as an element of inflammation in depression. On the other hand, animal model studies have found that DIO3 deficiency in brain cells increases thyroid hormones and reduces anxiety and depression. The results suggest a possible second direction of increased DIO3 expression, which in the brain may lead to decreased thyroid hormone levels and increased anxiety and depression symptoms. The obtained data on *DIO1* and *DIO3* gene expression indicate its variation in RDD and a complex possible mechanism of participation in the course of this disease. However, further research is needed to explain the changes in expression and the role of both DIO1 and DIO3 in depression-related mechanisms.

Gałecka E, Talarowska M, Maes M, Su KP, Górski P, Kumor-Kisielewska A, Szemraj . Expression levels of interferon-γ and type 2 deiodinase in patients diagnosed with recurrent depressive disorders. Pharmacological Reports 2018; 70: 133-138

My contribution to this paper involved working out the concept of research, research planning, performing experiments, analysing the results, performing a statistical analysis, reviewing the literature, preparing a manuscript, correcting the paper after review and formulating answers for reviewers. My percentage contribution is estimated at 80%.

As described above, the mechanisms and enzymes of thyroid hormone synthesis are under the influence of various factors, including molecules related to inflammatory processes. The correlation of expression of deiodinase synthesising enzymes with proinflammatory cytokines, such as interleukin-1 (IL-1), interleukin-6 (IL-6), tumour necrosis factor alpha (TNF-α), interferon-gamma (IFN-γ) or cyclooxygenase type 2, was observed. Data on DIO2 indicate an increase in the expression of this protein after incubation with proinflammatory cytokines or the action of bacterial lipopolysaccharide, which is also associated with inducing depressive behaviour. The expression of DIO2 and IFN-γ in the group of patients and healthy people was evaluated. It was assessed whether there is a correlation between the expression of these two genes and proteins. It was shown that changes of expression and concentration of type 2 deiodinase protein are observed in depression. A significantly lowered level and concentration of DIO2 was found in the group of patients compared to the control group. Neither the results of previous studies nor changes in the expression and concentration of IFN-γ nor correlations between the molecules studied were observed and confirmed.

Summary

Clarification of the complex mechanism of RDD and the participation of biological and biochemical agents is, and should be, one of the important objectives of contemporary scientific research regarding psychiatry. It is significant to search for and identify potential new genes or molecules that participate in and regulate processes and transformations the disorders of which have been observed in depression.

Analyses performed:

-identification of new genetic markers in RDD that can be identified in the peripheral material of patients;

-research studies conducted by our group discretely indicate the importance of genetic variants of the genes encoding DIO2 and DIO1 iodothyronine deiodinases in the development of depressive disorders or associated dysfunctions;

-the variants of *DIO1 and DIO3* genes do not seem to be relevant for the risk of RDD development and progression;

-the innovativeness of the research studies lies in the fact that they are among the first ones dealing with the issue of change in the expression of the above-mentioned *DIO1, DIO2, DIO3* genes and the concentration of their protein products in the peripheral material. The results of the studies confirm changes of mRNA expression in all three studied genes and differences in protein concentration between the patients with RDD and the control group of healthy volunteers.

In the light of the results obtained, changes in deiodinase expression may not only correlate with changes in thyroid hormone concentration, but may also be associated with depression-specific immune and inflammatory processes. The research results suggest that the role of expression of the genes encoding deiodinases and their polymorphisms in explaining the complex mechanism of development and course of RDD, further research and possible development of new therapeutic strategies should be taken into account.

References

1. Gilman SE, Sucha E, Kingsbury M, Horton NJ, Murphy JM, Colman I. Depression and mortality in a longitudinal study: 1952-2011. CMAJ 2017: 23;189(42):E1304-E1310
2. Lopizzo N, Bocchio Chiavetto L, Cattane N, Plazzotta G, Tarazi FI, Pariante CM, Riva MA, Cattaneo A. Gene-environment interaction in major depression: focus on experience-dependent biological systems. Front Psychiatry 2015: 8;6:68.
3. Rottenberg J. Emotions in Depression: What Do We Really Know? Annu Rev Clin Psychol 2017: 8; 13:241-263.
4. Gałecki P, Talarowska M. Neurodevelopmental theory of depression. Prog Neuropsychopharmacol Biol Psychiatry 2018; 80:267-272.
5. Maier W· Falkai P. The epidemiology of comorbidity between depression, anxiety disorders and somatic diseases. Int Clin Psychopharmacol. 1999;14 Suppl 2:S1-6.
6. Bauer M, Goetz T, Glenn T, Whybrow PC. The thyroid-brain interaction in thyroid disorders and mood disorders. J Neuroendocrinol. 2008;20: 1101-14.
7. Baumgartner A, Graf KJ, Kurten I, Meinhold H. The hypothalamic-pituitary-thyroid axis in psychiatric patients and healthy subjects: Parts 1-4, Psychiatry Res 24; 271-332.
8. Linnoila M, Lamberg BA, Potter WZ, Gold PW, Goodwin FK. High reverse T3 levels in manic an unipolar depressed women. Psychiatry Res, 1982; 6: 271-6.
9. Pinna G, Broedel O, Eravci M, Stoltenburg-Didinger G, Plueckhan H, Fuxius S et al. Thyroid hormones in the rat amygdala as common targets for antidepressant drugs, mood stabilizers, and sleep deprivation. Biol Psychiatry, 2003; 54: 1049-59.
10. Mazza M, Bria P, Taranto C, Janiri L, Mazza S. Mood, hormones and quality of life.Clin Ter. 2008; 159: 105-9
11. Samuels MH, Schuff KG, Carlson NE, Carello P, Janowsky JS. Health status, psychological symptoms, mood, and cognition in L-thyroxine-treated hypothyroid subjects. Thyroid 2007;17: 249-58.
12. Bonnin CM, Martinez-Aran A, Sanchez-Moreno J, Torrent C, Franco C, Pacchiarotti I, Vieta E. [Bipolar disorder, cognitive functioning and hypothalamic-pituitary-thyroid axis]. Actas Esp Psiquiatr. 2010; 38:223-8
13. Baumgartner A, Dubeyko M, Campos-Barros A, Eravci M, Meinhold H. Subchronic administration of fluoxetine to rats affects triiodothyronine production and deiodination in regions of the cortex and in the limbic forebrain.

Brain Res. 1994; 635: 68-74.
14. Eravci M, Pinna G, Meinhold H, Baumgartner A.Effects of pharmacological and nonpharmacological treatments on thyroid hormone metabolism and concentrations in rat brain. Endocrinology. 2000; 141: 1027-40.
15. Gałecki P. Peripheral markers of inflammation, oxidative & nitrosative stress pathways and memory functions as a new target of pharmacotherapy in depression. Prog Neuropsychopharmacol Biol Psychiatry. 2018; 80: 167.
16. Bernal J Action of thyroid hormone in brain. J Endocrinol Invest. 2002; 25: 268-88.
17. Köhrle J. Local activation and inactivation of thyroid hormones: the deiodinase family. Mol Cell Endocrinol 1999; 151: 103-119.
18. van der Deure WM[1], Hansen PS, Peeters RP, Kyvik KO, Friesema EC, Hegedüs L, Visser TJ. Thyroid hormone transport and metabolism by organic anion transporter 1C1 and consequences of genetic variation. Endocrinology. 2008; 149: 5307-14.
19. Canani LH, Capp C, Dora JM, Meyer EL, Wagner MS, Harney JW, Larsen PR, Gross JL, Bianco AC, Maia AL. The type 2 deiodinase A/G (Thr92Ala) polymorphism is associated with decreased enzyme velocity and increased insulin resistance in patients with type 2 diabetes mellitus. J Clin Endocrinol Metab. 2005; 90: 3472-8.
20. He B, Li J, Wang G, Ju W, Lu Y, Shi Y, He L, Zhong N. Association of genetic polymorphisms in the type II deiodinase gene with bipolar disorder in a subset of Chinese population. Prog Neuropsychopharmacol Biol Psychiatry. 2009; 33: 986-90.
21. Cooper-Kazaz R, van der Deure WM, Medici M, Visser TJ, Alkelai A, Glaser B, Peeters RP, Lerer B. Preliminary evidence that a functional polymorphism in type 1 deiodinase is associated with enhanced potentiation of the antidepressant effect of sertraline by triiodothyronine. .J Affect Disord. 2009; 116:
22. Philibert RA, Beach SR, Gunter TD, Todorov AA, Brody GH, Vijayendran M, Elliott L, Hollenbeck N, Russell D, Cutrona C. The relationship of deiodinase 1 genotype and thyroid function to lifetime history of major depression in three independent populations. Am J Med Genet B Neuropsychiatr Genet. 2011; 156B(5):593-9.
23. Peeters RP, van den Beld AW, Attalki H, Toor Hv, de Rijke YB, Kuiper GG, Lamberts SW, Janssen JA, Uitterlinden AG, Visser TJ. A new polymorphism in the type II deiodinase gene is associated with circulating thyroid hormone parameters.Am J Physiol Endocrinol Metab. 2005 Jul;289(1):E75-81.
24.

5. Other research achievements

5.1. Other research fields

5.1.1. The importance of oxidative stress in selected pathological conditions

Before obtaining the PhD in medical sciences, the subject of my research was oxidative stress. Together with the team from the Department of Clinical Chemistry and Biochemistry I participated in a study on free radicals generation, lipid peroxidation and antioxidant enzyme activity changes in patients after hip joint alloplasty. The results indicated increased generation of free radicals, increased activity of copper-zinc peroxide dismutase, catalase and glutathione peroxidase in patients suffering from hip joint degenerative disease after alloplasty. In another study I participated in the evaluation of the pro-oxidant and anti-oxidant system in various types of physical activity. Physical effort, apart from fulfilling a number of beneficial functions for the body, should be properly dosed and controlled because of the fact that it generates free oxygen radicals.

Mrowicka M., Gałecka E., Miller E., Garncarek P.: The influence of degenerative changes on free oxygen radical generation and lipid peroxidation (Polish: *Wpływ zmian zwyrodnieniowych na generacje wolnych rodników tlenowych i peroksydację lipidów).* Polski Merkuriusz Lekarski. 2008: 146:145-9

Mrowicka M., Garncarek P., Bortnik K., Gałecka E., Miller E., Śmigielski J.: Superoxide dismutase (CuZnSOD) activity in red blood cells in patients after hip joint alloplasty (Polish: *Aktywność dysmutazy ponadtlenkowej (CuZnSOD) w krwinkach czerwonych chorych po alloplastyce stawu biodrowego*). Polski Merkuriusz Lekarski, 2008, 143, 396-398

Mrowicka M., Garncarek P., Gałecka E., Miller E., Bortnik K., Żołyński K.: Activity of catalase and glutathione peroxidase in red blood cells of patients after hip replacement (Polish: *Aktywność katalazy i peroksydazy glutationowej w krwinkach czerwonych pacjentów po endoprotezo plastyce stawu biodrowego).* Kwartalnik Ortopedyczny, 2008, 2

Mrowicka M., Gałecka E., Malinowska K., Miller E.: ROS generation and lipid peroxidation in professional sportsmen (extreme sports condition) Medicina Sportiva 2008; 22: 56-60

In several review papers I was interested in the importance of free oxygen and nitrogen radicals in physiology, and in the structure and function of antioxidant enzymes of other non-enzymatic antioxidants, including flavonoids.

Gałecka E., Mrowicka M., Malinowska K., Gałecki P.: Free oxygen and nitrogen radicals in physiology (Polish: *Wolne rodniki tlenu i azotu w fizjologii*). Polski Merkuriusz Lekarski, 2008, 143, 446-448

Gałecka E., Jacewicz R., Mrowicka M., Florkowski A., Gałecki P.: Antioxidant enzymes – structure, properties, functions (Polish: *Enzymy antyoksydacyjne – budowa, właściwości, funkcje*). Polski Merkuriusz Lekarski 2008; 147:266-8

Gałecka E., Mrowicka M., Malinowska K., Gałecki P.: Selected non-enzymatic substances involved in the defence against excessive production of free radicals (Polish: *Wybrane substancje nieenzymatyczne uczestniczące w obronie przed nadmierną produkcją wolnych rodników*). Polski Merkuriusz Lekarski 2008; 147: 269-72

Miller E, Malinowska K, Gałecka E, Mrowicka M, Kedziora J. Role of flavonoids as antioxidants in human organism. Pol Merkur Lekarski. 2008 Jun;24(144):556-60

Due to my interest in oxidative stress in depression, I participated in the preparation of a paper describing the mechanisms leading to oxidative damage in the central nervous system.

Gałecki P., Florkowski A., Mrowicka M., Malinowska K., Gałecka E.: Calcium ions, glutamic acid, hypothalamic-pituitary-adrenal axis, calcium dependant ATPase as causes of oxidative damage in people suffering from depression – Part I (Polish: *Jony wapnia, kwas glutaminowy, oś podwzgórze-przysadka-nadnercza, ATP-aza zależna od wapnia jako przyczyny uszkodzeń oksydacyjnych u chorych na depresję – Część I*). Polski Merkuriusz Lekarski, 2007, 138, 466-468

Gałecki P., Florkowski A., Mrowicka M., Pietras T., Gałecka E.: Calcium ions, glutamic acid, hypothalamic-pituitary-adrenal axis, calcium dependant ATPase as causes of oxidative damage in people suffering from depression – Part II (Polish: *Jony wapnia, kwas glutaminowy, oś podwzgórze-przysadka-nadnercza, ATP-aza zależna od wapnia jako przyczyny uszkodzeń oksydacyjnych u chorych na depresję – Część II*). Polski Merkuriusz Lekarski, 2008, 139, 72-75

5.1.2. Evaluation of selected oxidative stress parameters in patients with depression taking into account the influence of antidepressant pharmacotherapy as well as therapy combined with acetylsalicylic acid

The contribution of oxidative stress, dysregulation of pro- and antioxidative balance, changes in antioxidant enzyme activity or concentration of non-enzymatic antioxidants in the aetiology of depression has been postulated and studied for years. The processes that lead to the overproduction of free radicals include increased glutamatergic transmission, monoamine oxidase activity, and mitochondrial dysfunctions, inflammation. In the research devoted to

evaluation of selected oxidative stress parameters, which were my doctoral dissertation, the following antioxidant enzymes of copper-zinc superoxide peroxidase, catalase, glutathione peroxidase and the concentration of malonyldialdehyde, which is one of the determinants of lipid peroxidation, were studied. The activity of enzymes and the concentration of malonyldialdehyde were studied in erythrocytes obtained from blood of the patients who were diagnosed with a major depressive episode before and after three months of fluoxetine treatment. It was shown that the activity of copper-zinc superoxide dismutase and catalase as well as the concentration of malonyldialdehyde were significantly higher than in the control group. After three months of therapy, however, no changes in the values of the above parameters were observed. A similar assessment was made for the group of patients treated with a combination of fluoxetine and acetylsalicylic acid for the first time in the world. The obtained results indicated significant changes in the values of the studied antioxidant enzyme activity and malonyldialdehyde concentration, which may indicate the role of acetylsalicylic acid in reducing the production of reactive oxygen species and pro- and antioxidative balance disorders in depression.

- Gałecki P, Szemraj J, Bieńkiewicz M, Florkowski A, Gałecka E. Lipid peroxidation and antioxidant protection in patients during acute depressive episodes and in remission after fluoxetine treatment. Pharmacological Reports. 2009, 61: 436-47 27

- Gałecki P, Szemraj J, Bieńkiewicz M, Zboralski K, Gałecka E. Oxidative stress parameters after combined fluoxetine and acetylsalicylic acid therapy in depressive patients. Human Psychopharmacology 2009;24:277-86

5.1.3. Evaluation of single nucleotide polymorphisms and expression of genes of selected immune and inflammatory factors in the aetiology of recurrent depressive disorders

The search for genetic factors that underlie depression did not provide a clear answer to the question regarding the genetic pathological mechanism of unipolar depression. In the light of current studies, it seems that depression develops as a result of many genetic factors with little effect.

An important process in depression aetiology is the inflammatory process and related enzymes such as myeloperoxidase (MPO), cyclooxygenase type 2 (COX-2), inducible nitric oxide synthase (iNOS) and secretory phospholipase IIA (sPLA-IIA).

One of the topics of my research was the search for the importance of single nucleotide polymorphisms and expression of enzyme-coding genes connected with an inflammatory process and induction of oxidative stress. Polymorphisms in genes were evaluated for the following enzymes: inducible nitric oxide synthase (iNOS), neuronal nitric oxide synthase (nNOS). Analyses have shown that there is a correlation between the presence of a genetic

variant and the risk of depression development. The distribution of genotypes and allele frequency, their influence on the risk of falling ill (ORdis) as well as the interdependence between the polymorphism and selected clinical indicators of RDD were evaluated. Having analysed the results of genotype distribution and allele frequency in genes for iNOS and nNOS among the affected patients, it was possible to determine that they differed significantly in comparison with healthy subjects. It has been proven that a polymorphism in both genes has an impact on the risk of RDD development. Studies evaluating the expression of genes encoding cyclooxygenase type 2, myeloperoxidase, inducible nitric oxide synthase, and secretory phospholipase A2 in peripheral blood cells showed significantly higher expression of all four genes at the mRNA level. This confirms the importance of an inflammatory process in the pathophysiology of depression. During the next stage of the research on genetic variants I participated in a study regarding the dependence of the functional polymorphism of the *NOS2A* gene. The -1026C/A variant is located in the promoter region of the gene, which is related to its level of expression. The study once again confirmed the correlation of the functional polymorphism of potential genes with a risk of depression. Differences were found in the distribution of genotypes among the studied groups. The obtained results indicated a determination of the risk of the disease depending on the allele possessed. The C allele has proven to be a positive risk factor (ORdis = 0.6; -CI 0.4-0.9) and the A allele a negative risk factor (ORdis = 1.6 -CI 1.1-2.3) for depression.

-Gałecki P, Maes M, Florkowski A, Lewiński A, Gałecka E, Bieńkiewicz M, Szemraj J. Association between inducible and neuronal nitric oxide synthase polymorphisms and recurrent depressive disorder. Journal Affective Disorders 2011, 129: 175-182.

-Gałecki P, Gałecka E, Maes M, Chamielec M, Orzechowska A, Bobińska K, Lewiński A, Szemraj J. The expression of genes encoding for COX-2, MPO, iNOS, and sPLA2-IIA in patients with recurrent depressive disorder. Journal of Affective Disorders 2012; 138: 360-366.

-Gałecki P, Maes M, Florkowski A, Lewiński A, Gałecka E, Bieńkiewicz M, Szemraj J. An inducible nitric oxide synthase polymorphism is associated with the risk of recurrent depressive disorder. Neuroscience Letters. 2010, 486: 184-7

5.1.4. Importance of genes involved in melatonin synthesis and mechanism of action in depression development

One of the hypotheses of depression development is that depression is a disease associated with low levels of melatonin. There are data in the literature indicating changes in melatonin concentration in patients with depression and a disturbance in signal transmission related to this molecule. Additionally, changes in daily rhythms and sleep disturbances are characteristic for the course of depressive disorders.

In cooperation with the Department of Adult Psychiatry and the Department of Medical Biochemistry, I participated in a study to evaluate the significance of functional polymorphisms of a single nucleotide (rs4446909, A/G; rs5989681, G/C) and the expression of the gene encoding acetylserotonin O-methyltransferase (ASMT) – an enzyme converting N-acetylserotonin to melatonin. Significant differences in the distribution of genotypes between the group of patients and controls were found, as well as a relationship between the presence of appropriate genotypes and the risk of depression. In the case of the rs4446909 polymorphism, the AA genotype was associated with a reduction of depression risk (ORdis 0.1; CI 0.03-0.58); similarly, in the case of the rs5989681 polymorphism, the GG homozygote decreased the risk of falling ill (ORdis 0.6; CI 0.4-0.97). Significantly decreased expression of the ASMT gene at the mRNA level was also observed in the affected patients in comparison with the control group.

Two polymorphisms (rs4753426, rs794837) of the gene encoding the MT2 melatonin receptor and mRNA expression were evaluated in another study. The analysis of allele frequency using logistic regression showed that having the C allele (ORdis 1.42; CI = 1.01-2.01.) of the rs4753426 variant increases the risk of depression. Relationships between the possession of an appropriate genotype and expression were found. However, no differences in mRNA expression were observed between patients and healthy subjects.

-Gałecki P, Szemraj J, Bartosz G, Bieńkiewicz M, Gałecka E, Florkowski A, Lewiński A, Karbownik-Lewińska M. Single nucleotide polymorphisms and mRNA expression for melatonin synthesis rate limiting enzyme in recurrent depressive disorder. Journal of Pineal Research 2010, 48: 311-7.

-Gałecka E, Szemraj J, Florkowski A, Gałecki P, Bieńkiewicz M, Karbownik-Lewińska M, Lewiński A. Single nucleotide polymorphisms and mRNA expression for melatonin MT_2 receptor in depression. Psychiatry Research 2011, 189: 472-474.

5.1.5. Assessment of the importance of selected processes and genetic factors related to cognitive function disorders in depression

Cognitive function disorders are often associated with dysfunctions in depression and a prognostic factor in the development of these disorders. Several processes characteristic of depression and related molecules can influence the onset of cognitive dysfunctions.

I participated in projects studying the contribution of genetic factors of their expression, biochemical processes and their relation to memory deficits in depression.

The results indicated increased expression of the following genes tested: *TNF, TNFRS1A, TNFRS1B,* and negative correlations between expression and operating memory,

executive functions, concentration, learning process efficiency and verbal fluency. Another study concerned gene encoding neuropsin, which is an endoprotease important for neuroplasticity processes – decreased expression of this gene correlates with cognitive function disorders. The results of the study indicate significant differences in gene expression between patients with the first episode of depression and those with subsequent episodes. Increased expression also correlates with reduced interpersonal abilities of the people with depression. The significance of oxidative stress in the deterioration of cognitive functions in depression was indicated by the results of a study assessing oxidation of thiol groups of antioxidant enzymes. Increased oxidation indicates a loss of antioxidant capacity of enzymes such as glutathione peroxidase. The study, in which I participated in cooperation with the Department of Adult Psychiatry and the Department of Pharmacology of the Medical University of Lodz, showed an increase in the oxidation of thiol protein groups and their correlation with the deterioration of cognitive functions such as operating memory or verbal fluency.

-Kinga Bobińska, Elżbieta Gałecka, Janusz Szemraj, Piotr Gałecki, Monika Talarowska. The role of TNF genes in depression and cognitive deficits. Acta Biochimica Polonica

-Talarowska M, Bobińska K, Gałecka E, Szemraj J, Gałecki P. **Human neuropsin gene and social cognition in depression. Neuropsychiatry 2016; 6 (6)**

-Galecki P, Talarowska M, Moczulski D, Bobinska K, Opuchlik K, Galecka E, Florkowski A, Lewinski A. Working memory impairment as a common component in recurrent depressive disorder and certain somatic diseases. Neuro Endocrinology Letters 2013;34:436-45.

-Gałecki P, Talarowska M, Bobińska K, Kowalczyk E, Gałecka E, Lewiński A. Thiol protein groups correlate with cognitive impairment in patients with recurrent depressive disorder. Neuro Endocrinology Letters 2013;34:780-6.

5.1.6. The role of selected genetic factors of the risk of depressive disorder development related to multidirectional and complex mechanism of disease development

As described earlier, depression is a disease entity with a complex and unexplained mechanism of development. A number of processes and molecules, associated with both the central nervous system and peripheral processes, have an impact on the development of the disease.

In cooperation with the Department of Adult Psychiatry and the Department of Medical Biochemistry, I took part in a study of polymorphisms of the gene encoding the KIBRA protein related to the regulation of memory processes, especially episodic memory, the disorders of which are a factor indicating the development of depression or may accompany

it. The obtained results did not, however, show any interrelation between the gene and RDD risk.

The importance of changes related to the functioning of the hypothalamic–pituitary–thyroid axis has been discussed and studied for many years. Particularly noticeable changes include glucocorticosteroid concentrations and changes in sensitivity to these hormones. Such changes may be related to genetic variants of glucocorticosteroid receptor genes. A study on the evaluation of three functional polymorphisms of the *NR3CI* gene showed that all three variants are significantly related to the risk of depression. Additionally, the haplotype analysis confirmed the importance of the examined gene in the determination of susceptibility to depression.

During the next stage of research, I participated in a project aimed at investigating the significance of genetic variants and gene expression as well as the concentration of the VEGF-vascular endothelial growth factor and one of its receptors for the development of depression.

The VEGF-vascular endothelial growth factor and the associated signal transmission mechanism are involved in numerous processes, such as neurogenesis and inflammation. Two these processes, namely neurogenesis disorders and activation of immune and inflammatory factors, are observed in depression. There is also evidence of decreased expression of VEGF in depression and its increase after the use of antidepressants.

The significance of genetic variants in both the VEGF encoding gene and its KDR receptor was demonstrated. Differences in distribution between patients and the healthy group were observed for the polymorphisms of both genes. For the VEGF gene, the haplotype analysis also indicated a haplotype that may determine the risk of developing depressive disorders. Significant differences were observed in the level of mRNA expression as well as in the protein concentration for VEGF and the studied receptor. The obtained results confirmed previous reports on the importance of the vascular endothelial growth factor in the depression mechanism.

-Gałecki P, Szemraj J, Talarowska M, Florkowski A, Bieńkiewicz M, Gałecka, Lewiński A. Single nucleotide polymorphism of the KIBRA gene in recurrent depressive disorders. Neuroendocrinology Letters 2010; 31: 97-102

-Gałecka E, Szemraj J, Bieńkiewicz M, Majsterek I, Przybyłowska-Sygut K, Gałecki P, Lewiński A. Single nucleotide polymorphisms of NR3C1 gene and recurrent depressive disorder in population of Poland. Molecular Biology Reports 2013; 40: 1693-9

-Gałecki P, Gałecka E*, Maes M, Orzechowska A, Berent D, Talarowska M, Bobińska K, Lewiński A, Bieńkiewicz M, Szemraj J. Vascular endothelial growth factor gene (VEGFA) polymorphisms

may serve as prognostic factors for recurrent depressive disorder development. Prog Neuropsychopharmacology & Biological Psychiatry. 2013; 45: 117-24.

-Gałecki P, Orzechowska A, Berent D, Talarowska M, Bobińska K, Gałecka E, Lewiński A, Maes M, Szemraj J. Vascular endothelial growth factor receptor 2 gene (KDR) polymorphisms and expression levels in depressive disorder. Journal of Affective Disorders 2013; 147: 144-9.

5.1.7. Searching for new molecular risk factors for thyroid cancer development

During my work at the Laboratory of Molecular Endocrinology of the Department of Endocrinology and Metabolic Diseases, in addition to the research regarding the factors involved in the development and course of depressive disorders, I also participated in research regarding the molecular background of thyroid cancer and expression of the genes related to pathways involved in carcinogenesis.

The biopsies collected from patients with papillary thyroid carcinoma showed an increase in COX-2 gene expression compared to the biopsies obtained from patients with non-toxic nodular goitre of the thyroid. This indicates the possible role of this gene in the pathogenesis of papillary thyroid carcinoma.

Another two projects concerned also papillary thyroid carcinoma. In the first study expression of the *PIK3CA* gene was studied. This gene encodes phosphatidylinositol kinase, the signal path of which is connected with apoptosis or cell proliferation processes. The expression of the *PIK3CA* gene in the material obtained from biopsies collected from patients with diagnosed papillary thyroid carcinoma and from patients with non-toxic nodular goitre of the thyroid (as control material) was evaluated in that study. Expression analysis showed increased values in the patients diagnosed with papillary thyroid carcinoma. The next gene analysed was the *NDRG2* gene, which belongs to the gene class inhibited by the N-Myc oncogene. The *NDRG2* gene is a new candidate gene for the development and progression of papillary thyroid carcinoma. Expression analysis was performed in postoperative material and macroscopically altered node, as in previous studies, using a method that evaluated expression in real time. The obtained results indicate reduced expression of the *NDRG2* gene in the case of pathological tissue compared to unchanged material.

-Krawczyk-Rusiecka K, Wojciechowska-Durczyńska K, Cyniak-Magierska A, Adamczewski Z, Gałecka E, Lewiński A. COX-2 expression in papillary thyroid carcinoma (PTC) in cytological material obtained by fine needle aspiration biopsy (FNAB). Thyroid Research 2011, 4: 3

-Mordalska A, Latek J, Ferenc T, Pomorski L, Gałecka E, Zygmunt A, Lewiński A. Evaluation of NDRG2 gene expression in primary papillary thyroid carcinoma and in metastases of this neoplasm to regional lymph nodes. Thyroid Research 2010, 30: 6

-Wojciechowska-Durczyńska K, Krawczyk-Rusiecka K, Cyniak-Magierska A, Zygmunt A, Gałecka E, Lewiński A. Relative quantification of PIK3CA gene expression level in fine-needle aspiration biopsy thyroid specimens collected from patients with papillary thyroid carcinoma and non-toxic goitre by real-time RT-PCR. Thyroid Research 2010 , 30: 5

5.1.8. Assessment of the role of iodothyronine deiodinases in chronic obstructive pulmonary disease

Continuing my research on the importance of iodothyronine deiodinases, I analysed serum concentrations of these proteins in patients with chronic obstructive pulmonary disease (COPD). It should be stressed that I was the first to perform such studies and the results showed significant differences in the concentration of type 1 deiodinase and type 3 deiodinase between the group of patients and a properly selected control group. The results are presented in the publication entitled "Assessment of serum levels of DIO1 and DIO3 in patients diagnosed with COPD" sent to Advances in Medical Science.

5.2. Participation in research projects

-Own topic awarded within the framework of own projects of the Medical University of Lodz, No. 502-17-663, entitled: "Pro- and antioxidant processes in erythrocytes in patients with severe depressive episodes"

-Grant awarded in the Ministry of Science and Higher Education Opus 4 Research Projects competition of the National Science Centre on the basis of the decision of the Head of the National Science Centre No. DEC-2012/07/B/NZ7/04212, 05.07.2013 - 04.07.2016, entitled: "Genes encoding iodothyronine deiodinases, expression at mRNA and protein levels in the complex risk mechanism of recurrent depressive disorders"

5.3. Awards and honours

Team Scientific Award of the First Degree given by the Rector of the Medical University of Lodz, 2012

Scientific Award of the Minister of Health in 2011 for a cycle of 7 publications concerning the evaluation of genes and mechanisms of inflammatory processes and connected with oxidative stress in depressive disorders; IF – 10.429

5.4. Membership in organization

European Thyroid Association

Polish Pharmaceutical association

Pharmaceutical Chamber in Łódź

5.5. Educational and organisational activity

Team Scientific Award of the First Degree given by the Rector of the Medical University of Lodz, 2012

Team Scientific Award of the Minister of Health in 2011 for a cycle of 7 publications concerning the evaluation of genes and mechanisms of inflammatory processes and connected with oxidative stress in depressive disorders; IF – 10.429

As an assistant at the Department of Clinical Chemistry and Biochemistry, I conducted classes and exercises in chemistry and biochemistry for students of the Faculty of Military Medicine. As a lecturer at the Laboratory of Molecular Endocrinology of the Department of Endocrinology and Metabolic Diseases, I conducted seminars with English-speaking students in the field of thyroid cancer genetics and classes with students of the Department of Cosmetology of the Faculty of Pharmacy of the Medical University of Lodz. I also lectured on the genetics of endocrine diseases for endocrinologists. I was a supervisor of three Master's theses:

- Agnieszka Kornacka, Master's thesis entitled: Comparative analysis of the impact of correctional and equalising classes on the posture of 3rd grade primary school pupils (Polish: *Analiza porównawcza wpływu zajęć korekcyjno-wyrównawczych na postawę ciała uczniów klas III szkół podstawowych*);
- Marta Leszko, Master's thesis entitled: Effectiveness of cosmetic methods in selected perimenopausal dermatoses (Polish: *Skuteczność metod kosmetologicznych w wybranych dermatozach wieku okołomenopauzalnego*);
- Monika Siuda, Master's thesis entitled: Evaluation of the quality of life of people with disabilities after spinal cord injury (Polish: *Ocena jakości życia osób niepełnosprawnych po urazie rdzenia kręgowego*).

6. Summary of publication record

My achievements to date include 35 publications, including 29 original papers and 6 review papers. The total score for original papers and review publications is IF 50,449, Ministry of Science and Higher Education 506. The current number of citations of my papers totals 436, Hirsch index 10, acc. to Web of Science Core Collection, 556, Hirsch index 13, acc. To Scopus as at 24 September 2018. The cycle presented as postdoctoral dissertation includes five original publications (IF 9,425; Ministry of Science and Higher Education 100). I am the first author in all the papers. After excluding the publications included in the postdoctoral cycle, my scientific achievements include 30 publications, including 24 original papers and 6 review papers, with a total score of IF 40.944, including 11,802 as the first author (Ministry of Science and Higher Education 406, including 124 as the first author). The results of my research were presented at two national conferences and two international ones.

Elżbieta Gałecka