Pályázat, projekt fő adatai	
azonosító	116128
típus	K
pénzügyi forrás	NKFI-1
pályázat nyelve	angol / English
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a pályázat címe angolul	Evaluation of thrombocytosis as predictive factor for survival in non-diabetic and diabetic patients
Kutatóhely neve	Belgyógyászati és Hematológiai Klinika (Semmelweis Egyetem)
projekt kezdete	2015-09-01
projekt vége	2021-02-28
Összefoglalás angol nyelven	**Summary of the research and its aims for experts** ***Describe the major aims of the research for experts.*** There is an increasing number of data suggesting that paraneoplastic thrombocytosis may promote metastatic progression. The pathomechanism is not completely elucidated yet and several hypotheses have been proposed; firstly platelets in patients with thrombocytosis induce tumor growth and angiogenesis via secretion of proangiogenic cytokines, secondly platelets play a role in metastatic progression by covering circulating tumor cells and protecting them from mechanic damage and the host's immune response, thirdly thrombocytosis is a paraneoplastic phenomenon as cytokines secreted by the tumor induce thrombopoiesis. However, it is clear that thrombocytosis is an excellent predictive factor regarding survival. It is widely known that diabetes mellitus has a great impact on platelet functions; the mean platelet volume is increased, TXA2 production is increased, CD40 ligands appear and the expression of adhesion molecules (CD31, CD36, CD49b, CD62P, CD63) and surface receptors (GP Ib and GP IIb/ IIIa) is increased. The aim of the study is to evaluate whether the predictive power of thrombocytosis related to solid tumors will be changed if diabetes mellitus is present. Not only the prognostic significance of thrombocytosis related to different tumors would be specified but also its pathomechanism would be evaluated. The following cytokines stimulating megakariocytopoiesis would be assessed in different solid tumors: IL-1α, IL-4, IL-6, IL-8, IL-11, G-CSF, GM-CSF, SCF and FLT-3 ligand. Not only the serum level would be measured but we would also evaluate whether the cytokines come from the primary tumor or the inflammatory ring around the tumor.

What is the major research question?
Describe here briefly the problem to be solved by the research, the starting hypothesis, and the questions addressed by the experiments.
The study evaluates the predictive power of thrombocytosis related to solid tumors regarding survival and pathomechanism. Reports have assessed the role of preoperative platelet count so far. In our present study we would like to evaluate the effect of tumor removal. If the platelet count changes then a strong correlation will be proved between thrombocytosis and the tumor. In the pathomechanism the role of IL-6 has been proposed in ovarian cancer. By measuring the serum level of IL1α, IL-4, IL-6, IL-8, IL-11, G-CSF, GM-CSF, SCF and FLT-3 ligand, we would like to clarify the role of other cytokines stimulating megakariocytopoiesis and thrombopoiesis in tumors. It is also interesting whether the different cytokines are originated from the tumor itself or the inflammatory ring around the tumor. The predictive power of thrombocytosis is affected by several factors from which diabetes mellitus may be the most interesting. It is well known that diabetes mellitus modifies platelet function through several factors (mean platelet volume, TXA2 production, appearance of CD40 ligands, expression of adhesion molecules such as CD31, CD36, CD49b, CD62P, CD63 and of surface receptors such as GP Ib and GP IIb/ IIIa). We would like to see whether diabetes mellitus influences the prognostic power of thrombocytosis related to solid tumors.

What is the significance of the research?
Describe the new perspectives opened by the results achieved, including the scientific basics of potential societal applications. Please describe the unique strengths of your proposal in comparison to your domestic and international competitors in the given field.
It is known that paraneoplastic thrombocytosis can actively promote metastatic progression and impair long-term survival. It is very important to clarify this subject because if a causal relationship exists we may be able to slow down metastatization by decreasing thrombocytosis and may improve patients' life expectancy. It is important in this aspect that a strong relationship between plasma IL-6, thrombopoietin and platelet count has been observed recently. Based on animal studies platelet count can be decreased by reducing IL-6 level (e.g. with siltuximab therapy). It raises the possibility that the active change of IL-6 level can result in a platelet count that is related to a slower metastatic progression. The observations above were made in ovarian cancer (Stone et al Paraneoplastic thrombocytosis in ovarian cancer. N Engl J Med. 2012 16; 610-8. IF: 51). In our study we would like to evaluate the findings of Stone et al in colorectal, esophageal, primary liver and pancreatic cancer. In addition to IL-6, we would like to extend our study to all cytokines stimulating megakariocytopoiesis. We would be first who evaluate how thrombocytosis changes following the removal of the primary tumor or in the presence of diabetes mellitus. Furthermore, we would also assess the expression of different cytokines of tumors in thrombocytosis related to primary tumors. Our study is the continuation of a previous international cooperation (Harvard / Boston, USA, Monmouth / Long Branch, USA, Technical University of Denmark, Dánia). Several articles hallmark this cooperation (Baranyai et al. the comparison if thrombocytosis and platelet-lymphocyte ratio as potential prognostic markers in colorectal cancer. Thromb Haemost. 2014; 111:483-90. IF: 6.01). Several external cohorts will be set up, thus, it will be a multicentrical study. Based on our study we may better understand the relationship of the tumor and thrombocytosis in different malignancies. We can also specify thrombocytosis as predictive marker in primary tumors. Our findings can be the starting point for further studies that aim to identify new therapeutic targets.

Summary and aims of the research for the public
Describe here the major aims of the research for an audience with average background information. This summary is especially important for NKFI in order to inform decision-makers, media, and the taxpayers.
Based on recent studies it seems to be more and more likely that elevated platelet count predicts a higher incidence of metastatic progression and worse life expectancy of patients in different malignancies. However, it is not clear yet whether it is only an occasional finding or there is a causal relationship between the elevated platelet count and the tumor. We would like to understand with our evaluations what kind of underlying mechanisms lead to the development of thrombocytosis in different malignancies. Our study would help us to get closer to answer this question. If a causal relationship will be confirmed the life expectancy of tumor patients could be improved by medically decreasing the platelet count..

OTKA

Type: K

Duration: 48 (2015-09-01 - 2019-08-31)

Budget plan: [redacted]

Identifier:	116128 K
Assigned panel:	KLINO
Project to supplement:	

Specialties:

International cooperation (organized, bidirectional); permission acquired; Equipment intensity (100%)

Title:	Evaluation of thrombocytosis as predictive factor for survival in non-diabetic and diabetic patients
Keywords:	thrombocytosis, diabetes mellitus, solid tumor, cytokine, survival

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Specialty and related panel:

100%	Clinics I. (Conservative)	Clinical Medicine

Panel proposed: Clinical Medicine (KLINO)

Interdisciplinary evaluation requested: No

Vá: Új Nemzeti Kiválósági Program 20-4-I jelentkezés

Feladó: DrkomplexU ÚNKP
Címzett: Zoltán Herold
Dátum: 2020. szeptember 7, hétfő 15:11
Tárgy: Vá: Új Nemzeti Kiválósági Program 20-4-I jelentkezés

Tisztelt Pályázó !

Az Ön pályázati azonosítója: ÚNKP-20-4-I-SE-17
Pályázatának szakértői összpontszáma: 212 pont
Ösztöndíjas időszak hossza: 12hónap

Tájékoztatom, hogy a Doktori Tanács elnökéből, a Doktorandusz Önkormányzat képviselőjéből és a doktori iskolák képviselőiből álló bizottság a doktori fokozatszerzések számának a Semmelweis Egyetem és az Országos Doktori Tanács által stratégiai célként elfogadott növelése érdekében valamint a Semmelweis Egyetem nemzetközi rangsorokban elért pozíciójának javítása érdekében pozitív elbírálásban részesítette azokat a pályázókat, akik D1 vagy Q1 besorolású folyóiratban első szerzős közleménnyel rendelkeznek.

Fenti szakmai indok alapján a támogatásra javasoltak rangsora nem feltétlenül a pályázaton elért összpontszámok alapján került meghatározásra.

Tájékoztatom, hogy az **Új Nemzeti Kiválóság Program** keretében meghirdetésre került ösztöndíj pályázatra **az Ön által benyújtott pályázat támogatásban részesült.**

A pályázati támogatás elnyeréséhez gratulálok.

Felhívom figyelmét az alábbiakra:

Az **ösztöndíjas jogviszony** feltételeinek történő megfelelést a Doktori Hivatal ellenőrzi és igazolja. (hallgatói jogviszony esetében a Neptun adatok alapján történik az ellenőrzés, így külön igazolás benyújtása nem szükséges, a posztdoktori kategória esetén a HR által kiállított jogviszony igazolás szükséges)

Tájékoztatom, hogy az ösztöndíjszerződés sablonja még nem áll rendelkezésre, az ösztöndíjszerződések megkötésének várható időpontja: 2020. október közepe.

Kérjük, hogy további kérdés esetén a Doktori Hivatal részére a titkarsag@phd.semmelweis-univ.hu email címre küldje el levelét.

Üdvözlettel:
Dr. Benyó Zoltán
a Doktori Tanács elnöke