



## Deliverable 3.3: Co-supervision of PhD thesis

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Workpackage:	3
Task:	3.3
Version:	2.0
Date:	29. 09. 2020



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## Basic information

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Project title	Strategies to strengthen scientific excellence and innovation capacity for early diagnosis of gastrointestinal cancers
Project acronym	VISION
Call	H2020-WIDESPREAD-2018-2020
Topic	WIDESPREAD-03-2018
Project type	Coordination and Supporting Action (CSA)
Grant Agreement No.	857381
Nature	<b>R</b> (Document, report - excluding the periodic and final reports)
Dissemination level	<b>PU</b> (Public, fully open, e.g. web)



## Executive summary

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Involvement of VISION partners in mentoring and co-supervision of PhD will increase the quality of education at universities, mainly medical and natural science faculties. PhD students of the Cancer Research Institute BMC SAS (Bratislava) are supervised by VISION project partners in the form of a co-supervision. So far seven PhD students have been allocated specific co-supervisors. Partner NILU supervises three PhD students, FhG and IRYCIS both each two PhD students. One of the IRYCIS co-supervised student will additionally be co-supervised by NKUA.



## 1 Description of work & main achievements

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Collaboration and networking between VISION partners will accelerate the personal and professional development of early stage researchers and medical doctors, impact the rate of success in internationally competitive research funding and high-quality peer-reviewed publications. Involvement of VISION partners in mentoring and co-supervision of PhD will increase the quality of education at universities, mainly medical and natural science faculties. PhD students of the Cancer Research Institute BMC SAS (Bratislava) are supervised by VISION project partners in the form of a co-supervision. So far seven PhD students have been allocated specific co-supervisors. Partner NILU supervises three PhD students, FhG and IRYCIS both each two PhD students. One of the IRYCIS co-supervised student will additionally be co-supervised by NKUA.

### 1.1 Co-supervision of PhD thesis

In the following please find details on the topic of the individual co-supervised PhD thesis and the co-supervisors.

#### 1.1.1 Co-supervision of PhD thesis #1

**PhD student:** Kristína Kopecká, MSc.

**Topic of PhD thesis:** Distribution, accumulation and biological effects of gold nanoparticles in vivo.

Annotation: Targeted drug delivery is one of the main fields of medicine where nanotechnology can substantially contribute to the breakthrough in treatment efficacy of various diseases. Elucidation of relations that determine enhanced affinity of nanomaterials toward certain organ/tissue is therefore in a spotlight of nanotherapy research. Very promising nanomaterials for targeted delivery are noble metals like gold. Gold nanoparticles show almost no acute toxicity and their unique optical features enable to monitor them in the body. Despite significant benefits nanomaterials hold for nanomedicine, the questions concerning their bio-safety remain insufficiently explored. These are mainly their interactions with cells on the molecular level, mechanism of distribution, accumulation and elimination from the body, as well as their possible biological adverse effects emerging from a long-term exposure. Deeper understanding of these natural patterns will significantly contribute to the development of safer and more effective nanotherapeutics.

**Supervisor:** Andrea Bábelová, PhD. - Cancer Research Institute BMC SAS, Bratislava

**Co-supervisor/consultant:** Dr. rer. nat. Yvonne Kohl – Fraunhofer-Institut für Biomedizinische Technik IBMT, Sulzbach, Germany (FhG)

#### 1.1.2 Co-supervision of PhD thesis #2

**PhD student:** Lucia Bálintová, MSc.

**Topic of PhD thesis:** Biological safety of innovative nanotherapeutics with potential application in regenerative medicine.

Annotation: Development of novel therapeutically active wound dressings which provide the wound protection as well as wound healing promotion has an advantageous potential for clinical applications. Our goal is to assess the biosafety of prepared innovative nanohydrogels in in vitro and in vivo conditions. Nanogel integrates protective (nanohydrogel) and healing



functions (iron oxide nanoparticles and targeted miRNA) within one nanocomposite structure; and detailed characterization of nano:bio interactions will contribute to elucidate the mechanisms of action of nanogels in the biological system.

**Supervisor:** Dr. rer. nat. Monika Šramková, PhD - Cancer Research Institute BMC SAS, Bratislava

**Co-supervisor/consultant:** Dr. rer. nat. Yvonne Kohl - Fraunhofer-Institut für Biomedizinische Technik IBMT, Sulzbach, Germany (FhG)

### 1.1.3 Co-supervision of PhD thesis #3

**PhD student:** Jana Hricovíniová, MSc.

**Topic of PhD thesis:** New precursors of pharmaceuticals based on nitrogen heterocyclic compounds and glycoconjugates: structure-biological activity relationship analysis.

Annotation: Development of new drugs with increasing specificity and sensitivity is one of the main aims in the field of medical research. Significant attention has received nitrogen-containing heterocycles that are part of many natural compounds (e.g. nucleic acids, alkaloids, antibiotics, barbiturates). Quinazoline and quinazolinone-based compounds represent a unique class of heterocyclic compounds displaying a wide range of therapeutic and pharmacological properties such as, anticancer, antibacterial, antiviral, antifungal, anti-inflammatory, or antimalarial activities. The aim of this study is evaluation of biological activities of new synthetic quinazolinone derivatives in vitro. A series of new derivatives will be tested by various chemical, biochemical and molecular biology assays utilizing kidney cancer and non-cancer cell lines.

**Supervisor:** Dr. rer. nat. Katarina Kozics, PhD. - Cancer Research Institute, Biomedical Research Center SAS, Bratislava

**Co-supervisor/consultant:** Dr. rer. nat. Mária Dušinská, DSc. - Norwegian Institute for Air Research, Oslo, Norway (NILU)

### 1.1.4 Co-supervision of PhD thesis #4

**PhD student:** Verona Buociková, MSc.

**Topic of PhD thesis:** Nanocarrier Mediated Multimodal Anticancer Therapy

Annotation: In the last decade, significant progress has been made in the use of the properties of nanoparticles for medical applications, especially in the field of anticancer treatment. The new generation of nano-drugs not only ensures a synergistic effect of several substances and specific targeting of therapy but also enables an increase in the sensitivity of resistant cell populations and monitoring of drug accumulation in the tumor. The goal is the development of a new generation of multi-functional nano-drug that combines diagnostic and therapeutic potential within one nanostructure. It has four key components: 1. surface ligands for targeting tumor cells, 2. a diagnostic component in the form of inorganic nanocrystals, 3. a cytotoxic component, and 4. an epigenetic drug as a chemosensitizer. As part of the dissertation, the student will realize in vitro experiments aimed at evaluating the expression of stem cell markers on tested cell lines, testing and evaluating the response to treatment in cell lines, and evaluating the safety and efficacy of the developed drug before its in vivo application. In this work, she will learn to reliably use the whole spectrum of molecular biological methods such as flow cytometry, cell culture in 2D and 3D conditions, immunohistochemical staining, western blot, real-time PCR and many others.



**Supervisor:** Bozena Smolkova, PhD. – Cancer Research Institute, Biomedical Research Center SAS, Bratislava

**Co-supervisor/consultant:** Dr. rer. nat. Mária Dušinská, DSc. - Norwegian Institute for Air Research, Oslo, Norway (NILU)

### 1.1.5 Co-supervision of PhD thesis #5

**PhD student:** Michaela Blažičková, MSc.

**Topic of PhD thesis:** Relationship between structure and biological activity of newly synthesized thymol derivatives in colorectal in vitro model.

Annotation: Beneficial effects of thymol (TY), a naturally occurring phenol monoterpene of essential oil from thyme, on human health are well known for many years. The proposed project is focused on the synthesis of hydrophilic derivatives of TY while the antioxidative and antiproliferative properties as well as the effective cellular uptake will remain intact. Using comprehensive approaches from biochemistry, biology, and molecular biology will enable us to assess the biological effects of these derivatives depending on their molecular structure. The project will contribute to gain an insight into the molecular mechanisms of action of hydrophilic TY derivatives. The biological activity will be studied using 2D and 3D colorectal cell models cultured in vitro.

**Supervisor:** Dr. rer. nat. Katarína Kozics, PhD. - Cancer Research Institute BMC SAS, Bratislava

**Co-supervisor/consultant:** Dr. rer. nat. Mária Dušinská, DSc. - Norwegian Institute for Air Research, Oslo, Norway (NILU)

### 1.1.6 Co-supervision of PhD thesis #6

**PhD student:** Kristina Ploth, MSc.

**Topic of PhD thesis:** Advanced in vitro and in vivo models derived from primary tumour tissue as tool for preclinical research

Annotation: Models based on primary tumour cells such as organoids and patient-derived xenografts (PDX) are recently the most relevant preclinical systems for evaluation of efficacy of anticancer approaches as well as for studies focused on cancer cell biology, chemoresistance and metastasis. Based on existing cooperation with clinicians we will use vital samples of tumour tissue obtained at surgical resection of colon cancer for preparation of organoids and PDX. Subsequently, these models will be used for evaluation of efficacy and safety of combined therapy targeted via nanocarrier as well as for study of mechanisms of chemoresistance and metastasis.

**Supervisor:** Dr. rer. nat. Miroslava Matúšková, PhD. – Cancer Research Institute, Biomedical Research Center SAS, Bratislava

**Co-supervisor/consultant:** Maria-Laura Garcia-Bermejo, PhD. - Instituto Ramon y Cajal de Investigación Sanitaria, Madrid, Spain (IRYCIS)

### 1.1.7 Co-supervision of PhD thesis #7

**PhD student:** Peter Dubovan, MD

**Topic of PhD thesis:** Management of postoperative pancreatic fistula



Annotation: Postoperative pancreatic fistula (POPF) is the most common postoperative complication after pancreatic resection. Even though, there are multiple works dedicated to this problem, there is still missing knowledge of all risk factors contributing towards POPF and there is missing unanimous management preventing creation of POPF or management of POPF after its creation. In the surgical world there are trends towards minimising the use of intraabdominal drainage. This trend is visible also in pancreatic surgery, however in our current practise we routinely use intraabdominal drainage in pancreatic surgery and we think we have very good results regarding overall morbidity and mortality.

Therefore, in this work we aim to conduct retrospective analysis of our single center cohort in the years 2015-2020. We want to compare our data with the data from current literature and eventually create the baseline for a new protocol/recommendations with a prospective phase of the study.

Potential expansion: The additional research goal broadening the focus of the study towards practical aspects of the intervention is related to the routine use of postsurgical intraabdominal drainage in pancreatic adenocarcinoma and potential understanding of the underlying disease, its therapy and impact on further prognosis of patients. There is ongoing discourse focused on radicality in pancreatic cancer surgery, concentrating among else on the significance of the role of peritoneal lavage in overall survival, with unanswered questions on the key related factors impacting survival. Our research would explore utilization of the fluid from the intraabdominal drainage, to identify either carcinomatous cells or biomarkers, to expand our understanding of the pathophysiological processes after surgery and optimise therapeutical interventions based on this insight. Our assumption is that this could help confirm the impact and most optimal administration of excessive peritoneal lavage, nowadays conducted with saline, but maybe in the future with more effective solutions and ultimately increase the effectiveness of oncological treatment and prognosis for patients.

**Supervisor:** Assoc. Prof. Daniel Pinďák, MD, PhD. – Slovak Medical University, Bratislava

**Co-supervisor/consultant:** Prof. Manousos M Konstadoulakis - National and Kapodistrian University of Athens (NKUA), Athens, Greece; and Julie Earl, PhD. - Instituto Ramón y Cajal de Investigación Sanitaria, Madrid, Spain (IRYCIS)

## 2 Deviation from the work plan

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There are no deviations from the work plan.

## 3 Conclusion

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Seven PhD students with specific reserach topics as well as specific co-supervisors of the consortium partners have been identified. Partner NILU supervises three PhD students, FhG and IRYCIS both each two PhD students. One of the IRYCIS co-supervised student will additionally be co-supervised by NKUA.