GYNOCARE

European network for Gynaecological Rare Cancer Research: From Concept to Cure (CA18117)

GYNOCARE Management Committee Meeting
Skopje, North Macedonia – 18th September 2022

Action Chair: Prof Jean Calleja-Agius

cost
EUROPEAN COOPERATION
IN SCIENCE AND TECHNOLOGY

COST is supported by the EU Framework Programme Horizon 2020

Management Committee Meeting
Sunday 18th September 2022 from 16.30 to 18.30
(by invitation only to MC members and substitutes)

1. Welcome to participants, verification of the quorum and adoption of agenda
2. Information to the MC
a) Recap of the minutes of the last meeting, e-votes and matters arising since the last meeting
b) Action Membership: New Specific Organisations and COST Members represented in the MC
c) Action Participation: WG membership and applications, New MC members/Observers and provisional substitution.
d) Budget status: summary from the Grant Holder.
3. Follow up and discussion on the
a) Action management: structure, leadership positions and other supporting roles. Mandates to the Core Group
b) Implementation of the COST Excellence and Inclusiveness Policy
c) Grant Awarding by the Action
d) Progress of each working group
e) Science Communication Plan – Dr Vera Dimitrievska
f) Progress on MoU Objectives, WG tasks, deliverables, and Goals for the current GP.
4. Planning
a) Revision of Work and Budget Plan of the current GP
b) Draft plans for the following GP(s).
c) Upcoming activities
d) GYNOCARE Conference in Naples, February 2023
e) Extension of the Grant Period till September 2023
f) 2nd GYNOCARE Training School in Bulgaria, April 2023
g) Final conference in August 2023
h) Ideas for application of Innovation Grant – Prof Evzen Amler
5. Monitoring and Reporting to the COST Association
6. AOB
7. Summary of MC decisions
8. Closing

Management Committee Meeting Minutes

Date: 24th May 2022: 14.30 till 16.00 (CET)

Venue: Hybrid meeting, Valletta Campus, University of Malta, Malta

Minutes:

Welcome by Chair

Approval of minutes from MC meeting of 26th October 2021

Introduction of new member countries

Status update on Action Website and social media

Outputs of COST Action during this grant period

Decision to include rare types of breast cancer in the list of rare gynaecological cancers

Decision for application for 6 months' extension

Decsion for location of upcoming meeting : Training School and Management Committee Meeting in Skopje, North Macedonia, September 2022

E-voting since the previous MC meeting

Request for a 6 month extension of the GYNOCARE COST Action Jean Calleja Agius	MC-Voting	Closed	✔ Approved	29/08/2022 05/09/2022
STSM application - Dr Nikolai Pace Jean Calleja Agius	MC-Voting	Closed	✔ Approved	09/09/2022 16/09/2022

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Aims

Unique network between key stakeholders covering five distinct domains:

- WG1: Basic research on rare gynaecological cancer
- WG2: Biobanking
- WG3: Legal and regulatory issues
- WG4: Industrial dimension to bridge the gap between translational research and pharmaceutical/biotechnology companies
- WG5: Designing high-quality, international, and innovative clinical trials

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Prof C. Simon Herrington
WG 1 Leader
Cancer Research UK Edinburgh Centre, UK
simon.herrington@ed.ac.uk
Dr Sharon O'Toole
WG2 Leader
Trinity St James's Cancer Institute, Trinity College Dublin, Ireland shotoole@tcd.ie
Dr Olga Tzortzatou
WG 3 Leader
Biomedical Research Foundation, Academy of Athens, Greece
olga_tzortzatou@yahoo.gr
Prof Antonio Giordano
WG 4 Leader
Sbarro Institute, Temple University, USA & University of Siena, Italy
giordano12@unisi.it
Dr Klejda Harasani
WG 5 Leader
University of Medicine Tirana, Albania
klejda.harasani@umed.edu.al

Output of Working Groups to date

- WG1 – 12 publications, 3 STSMs, 6 Virtual Mobility Grants, 1 ITC conference grant
- WG2- Biobanking 4 Virtual Mobilities, 1 STSM (October 2022)
- WG3 -2 Virtual Mobilites
- WG4 – Future Conference in Naples (March 2023)
- WG5 – 1 Virtual Mobility, 1 publication (being submitted)

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Focus on:

- capacity-building on rare gynaecological cancer by connecting high-quality scientific communities in various disciplines, existing networks, policy-makers, industrial partners, and patient organisations across Europe and beyond;

- coordinating, and contributing to the development of a research roadmap dedicated to connect innovative basic research to harmonised biobanking to ‘smarter’ clinical trials;

- the development of a platform for sharing best practices, including funding roadmap and legal/ethical requirements, in rare gynaecological cancers, aiming to advice policy-makers and other key stakeholders;

- providing equal networking opportunities for early-stage researchers, and other talented young professionals.

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Funding available for:

- Open access collaborative publications
- Attendance and participation in conferences
- Organisation and participation in training schools
- Short term scientific missions
- Virtual networking

Preference given to early stage career investigators and trainees, and applicants from ITC

If interested, email: jean.calleja-agius@um.edu.mt or visit us on www.gynocare.net

Approved Budget 2021-2022

(till October 2022)

MAXIMUM BUDGET	159,500	
Summary Budget		**Amount**
Networking Tool Quant. Budget		**EUR**
Meetings (MC)		
Virtual/Hybrid meeting	expenses for technical set up	0
2 MC meetings - March and August plus 2 physical core group meetings	by invoices/ max 10k	41695
Core group meeting - virtual		
Working group meeting x 5 - virtual		
1 Training School	by invoices/ max 10k	10,000.00
Conference	by invoices/ max 10k	10,000.00
Short Term Scientific Missions (STSM)	potential 4 STSM between safe corridors	10,000.00
ITC Conference Grant - inc virtual conference fees	4 participants x Eur 500/conference	2,000.00
COST Action Dissemination		
Scientific Publications		40,000.00
Flyers, Video dissemination to public		2,000.00
Conference attendance		2,000.00
Website hosting and maintenance		2,000.00
Virtual Networking Support Grant		4,000.00
Virtual Mobility Grants	10 x Eur 1500	15,000.00
Other Expenses Related to Scientific Activities (OERSA)	bank charges, licence fees for virtual communication tools	
SCIENCE EXPENDITURE		**138,695.00**
Financial and Scientific Administration and Coordination (FSAC) - MAX. 15%		20,804.25
TOTAL GRANT		**159,499.25**

New COST Budget Allocation November 2022 till September 2023

- 132,000 Euros (includes 15% FSAC) = **112,000 Euros**

Working Budget Plan:

- 2 day Conference in Naples, Italy in February 2023
- 3 day Training School in Bulgaria in 2023 (date to be confirmed)
- Final Conference in 2023 (date and location to be confirmed) – offers from Serbia or co-located in Bulgaria
- At least 2 STSMs
- More publications

Open Access Publications

Since October 2020, 12 collaborative open access publications have been published:

- 2 papers in Cancers (IF: 6.6)
- 5 papers in International Journal of Molecular Sciences (IF: 5.9)
- 1 in Biomedicines (IF: 6.01)
- 1 chapter in Springer book series
- 3 published in other open access journals

Available at https://gynocare.net/research-output/

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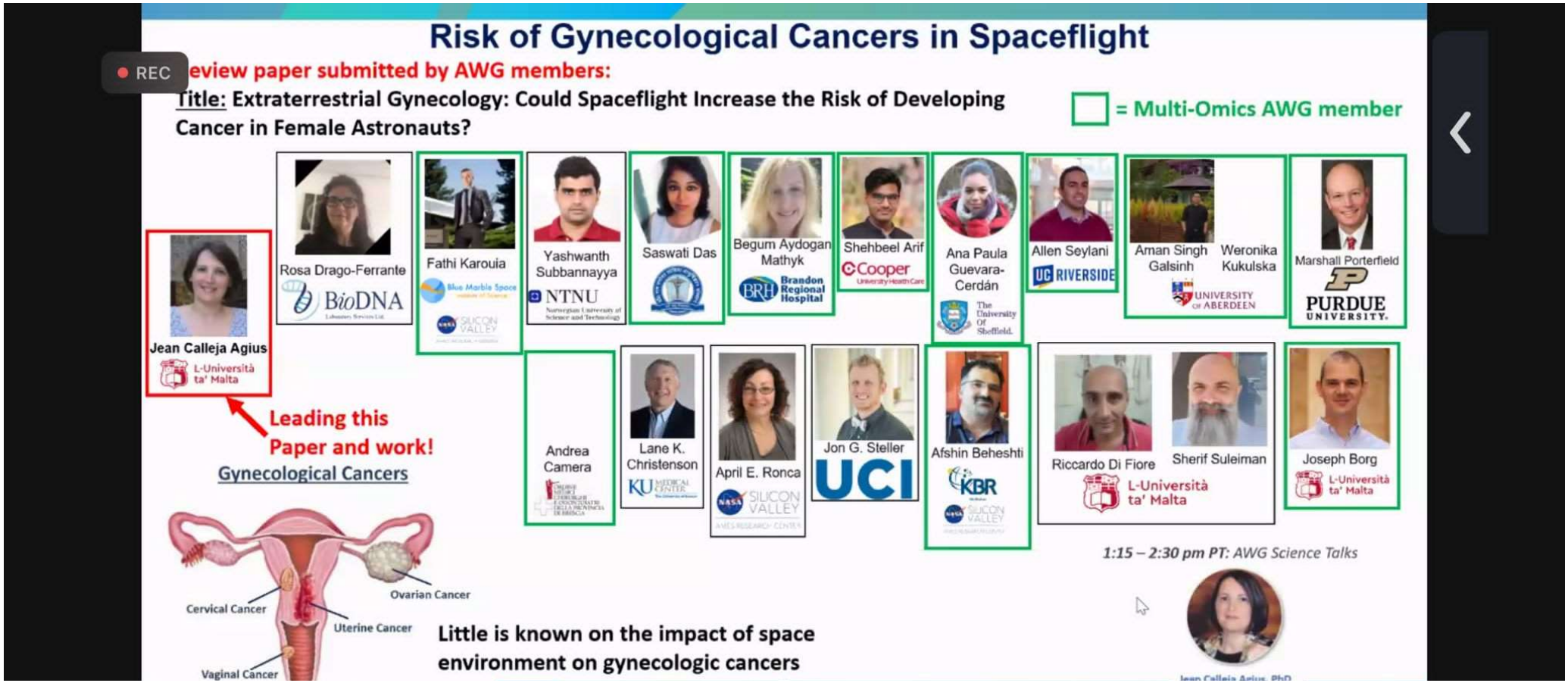
Colloaboration with NASA (USA)



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International Journal of *Molecular Sciences*

MDPI

Extraterrestrial Gynecology: Could Spaceflight Increase the Risk of Developing Cancer in Female Astronauts? An Updated Review

Rosa Drago-Ferrante [1,†], Riccardo Di Fiore [3,4,†], Fathi Karouia [2], Yashwanth Subbannayya [5,†], Saswati Das [6,†], Begum Aydogan Mathyk [7,†], Shehbeel Arif [8], Ana Paula Guevara-Cerdán [9], Allen Seylani [10], Aman Singh Galsinh [11], Weronika Kukulska [12], Joseph Borg [13], Sherif Suleiman [3], D. Marshall Porterfield [14], Andrea Camera [15], Lane K. Christenson [16], April E. Ronca [17], Jon G. Steller [19], Afshin Beheshti [18,*] and Jean Calleja-Agius [3,*]

More Open Access Collaborative papers submitted:

- Epidemiological paper led by Bulgarian team: Dr Angel Jordanov & Dr Mariela Vasileva-Slaveva

- Case Report led by Maltese team: Dr Andee Agius

- Systematic Review led by lead of WG5: Prof Klejda Harasani

Appeal for more.....

- At least 3 authors from 3 COST countries
- Case reports, original research, reviews....
- Related to rare gynaecological cancers

Virtual Mobility Grants: 2021-2022

- **Dr Rosa Drago Ferrante from Malta**

Title of VM: Spaceflight and risk of Gynaecological Cancers, including Rare types

Duration of VM: 01/04/2022 till 30/05/2022

- **Dr Angel Yordanov from Bulgaria**

Title of VM: Feasibility, regulations and sustainability of virtual biobanks in Eastern Europe

Duration of VM: 02/06/2022 till 28/07/2022

- **Prof Noya Galai from Israel**

Title of VM: Virtual Biostatics Clinic

Duration of VM: 05/06/2022 till 26/09/2022

- **Dr Francesco Pegreffi from Italy**

Title of VM: Telemedicine to Evaluate the Interplay Between Quality of Life and Sarcopenia in the Management of Rare Gynaecological Cancer

Duration of VM: 08/07/2022 till 30/09/2022

Virtual Mobility Grants: 2021-2022 (continued)

- **Prof Klejda Harasani from Albania**

Title of VM: Compilation of a Clinical trialreference depository established (finalized and running) for rare gynecological cancers

Duration of VM: 08/07/2022 till 30/09/2022

- **Prof Yashwanth Subbannayya from Norway**

Title of VM: Studying the potential effects of space flight on rare gynecological cancers using multi-omics approaches

Duration of VM: 01/08/2022 till 30/09/2022

- **Dr Vera Dimitrievska from North Macedonia**

Title of VM: The creation of an online resource for training on pathology of rare gynaecological cancers

Duration of VM: 08/08/2022 till 01/10/2022

Virtual Mobility Grants for 2021-2022

More available (max 1500 Euros each):

https://gynocare.net/uncategorized/new-call-for-virtual-mobility-grants-in-2022/

All must be completed by the 30th October 2022

Short Term Scientific Missions (STSMs)

3 successful applications so far:

- Dr Christian Camenzuli (Malta) at TU Delft in the Netherlands – Development of a safer Verress Needle for pelvic surgery
- Dr Chiara Tommaro (Italy) - Displaying the Link between Human Papillomavirus Positive Cervical Cancer and Laryngeal Cancer throughout the involvement of miR-223: a Potential Early Diagnostic Biomarker
- Dr Nikolai Pace (Malta) to visit Trinity College Dublin – Biobanking

1 more available (max 2500 Euros) – must be completed before end of October 2022

https://gynocare.net/uncategorized/new-call-for-short-term-scientific-missions-in-2022/

ITC grants and Dissemination grants

- One successful ITC grant Application: Dr Milan Paul Kubelac to present at ESGO in October 2023
- More available on condition: ITC country, under age of 40 years

- Dissemination Grants: anyone can apply, but must be an oral presentation (not poster)

- Must be completed by end of October 2022 for this grant period

Website

www.gynocare.net

600 users over the past 90 days

News, Events, Applications for VMs and STSMs

Links to research output

Social Media

- Facebook

GYNOCARE COST Action: 220 followers

- Twitter
- Linked in
- Instagram

- More news items to share – cite GYNOCARE Cost Action (CA18117)

- Contact Science Communication Officer for GYNOCARE: Vera Dimitrievska

Deliverables achieved:

- D1.2: Annual meeting summary. Once a year all the consortium will meet and present the work carried out during the year, after which a meeting summary will be prepared.
- D2.2: European network of gynaecological pathologists established (virtual network from the existing European biobanks for rare gynaecological malignancies) –**Survey on biobanking to be redistributed**
- D3.1: A main document showing all the different national legal requirements valid for the EU and non-EU Countries within Europe – **Survey on legal aspects to be redistributed**

Pending deliverables – work in progress

- D5.1: Clinical trial reference depository established (i.e. finalised, running, and planned) that are coordinated or organised by the network : systematic review has been submitted for publication
- D1.5.1: Training schools, that could be organised every year if funding allows, will provide the consortium with specific knowledge needed for the specific strategic lines : currently in North Macedonia, next in Bulgaria
- D2.3: Harmonisation of existing tools for digital pathology. The existing experience will be brought together in order to facilitate the central histological review, as also to be able to discuss basic research results performed on this samples : Training school and VM, future work
- D2.4.1: Established training curriculum in the diagnosis of rare cancers, to be used for the first online training courses for young pathologists : Training school and VM, future work

D5.2.1: Regular meetings where all the researchers meet in different European cities to discuss new clinical trials, harmonisation strategies or to receive some training

- September 2022 – North Macedonia
- February 2023 – Italy
- 2023 (?date)– Bulgaria
- 2023 (?date/location)– Final conference
- Workshop by WG2 – led by Dr Sharon O'Toole -?combined with conference or training school

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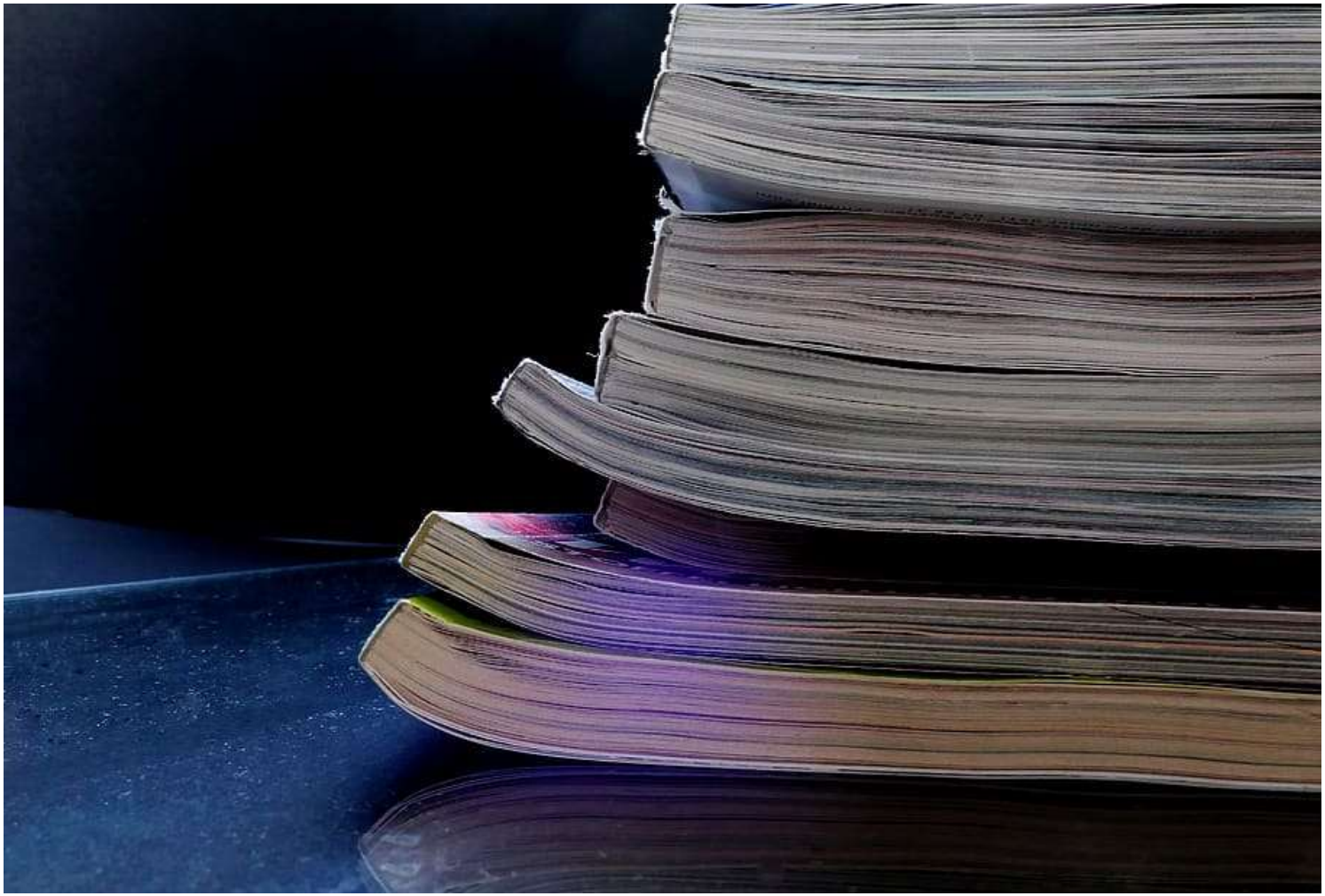
Book Proposal



- D4.1: Informative booklet for dissemination to the industries. After 6 months this tool will be available, including information on the overall structure and of all the activities of potential interest for the companies

- Open access book on Rare Gynaecological Cancers

Welcome to Naples, Italy
for the next 2-day GYNOCARE conference
FEBRUARY 2023
Presentation by Prof Francesca Pentimalli

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Ph credit: www.naporama.it

Naples is the regional capital of Campania and one of the largest in Italy spanning approximately 20 miles. Naples is easily reached by train (it is less than two hours from Rome), through the local city airport, or by the sea.

Naples was founded by the Greeks and has been one of the oldest continuously inhabited urban areas in the world. First known as Parthenope, Naples became an important center of Magna Grecia and a significant cultural centre under the Romans. It's been the capital of the Kingdom of the Two Sicilies until Italy unification in 1861.

There's a lot to see both in Naples and the surroundings (including Pompei –the old roman city buried in the eruption of Mount Vesuvius in AD79 – or the beautiful Amalfi coast, the Flegrean fields and the Islands of Ischia, Procida and Capri). It is only few miles from the beautiful Real Palace of Caserta the largest royal residence in the world.

Neapolitan cuisine is mostly associated to the PIZZA but there also many other local dishes from mozzarella to babà and sfogliatelle….. be prepared to gain some pounds

Real Teatro di San Carlo is an opera house in Naples located adjacent to the central Piazza del Plebiscito, and connected to the Royal Palace. It is the oldest continuously active venue for public opera in the world, opening in 1737, decades before both the Milan's La Scala and Venice's La Fenice theatres.

The National Archaeological Museum of Naples (MANN) is an important Italian archaeological museum, particularly for ancient Roman remains. Its collection includes works from Greek, Roman and Renaissance times, and especially Roman artifacts from nearby

Museo di Capodimonte is an art museum located in the Palace of Capodimonte, a grand Bourbon palazzo in Naples, Italy. The museum is the prime repository of Neapolitan painting and decorative art, with several important works from other Italian schools of painting, and some important ancient Roman sculptures. It is one of the largest museums in Italy.0

This 2 day conference, organized by Prof Antonio Giordano (leader of WG4) and Prof Francesca Pentimalli, will bring together eminent scientists and clinicians in the field of gynecological rare cancer.

The focus of the meeting will be on recent advancements in gynecological rare cancers from diagnosis to treatment and will highlight the importance of translational research and networking activities.

A tentative list of speakers includes:

- Prof Sergio Sandrucci (Visceral Sarcoma Unit, CDSS - University of Turin Italy) - sergio.sandrucci@unito.it
- Prof Vesna Kesic (ESGO, University of Belgrade, Serbia) -vek1@mts.rs
- Prof Michele Caraglia (University of Campania, Italy) - michele.caraglia@unicampania.it
- Prof Martin Persson (University of Kristianstad, Sweden) - martin.j.persson@hkr.se

Future planning

- Extension of the Grant Period till 11th September 2023 (granted)

- 2nd GYNOCARE Training School in Bulgaria, 2023 –
Dr Mariela Vasileva-Slaveva

- Final 3 day conference in 2023 – ? Location

- Ideas for application of Innovation Grant – Prof Evzen Amler

Idea for GYNOCARE Innovation Grant: Functionalized nanofibers for modern theragnostics and personalized medicine

Prof. Evžen Amler

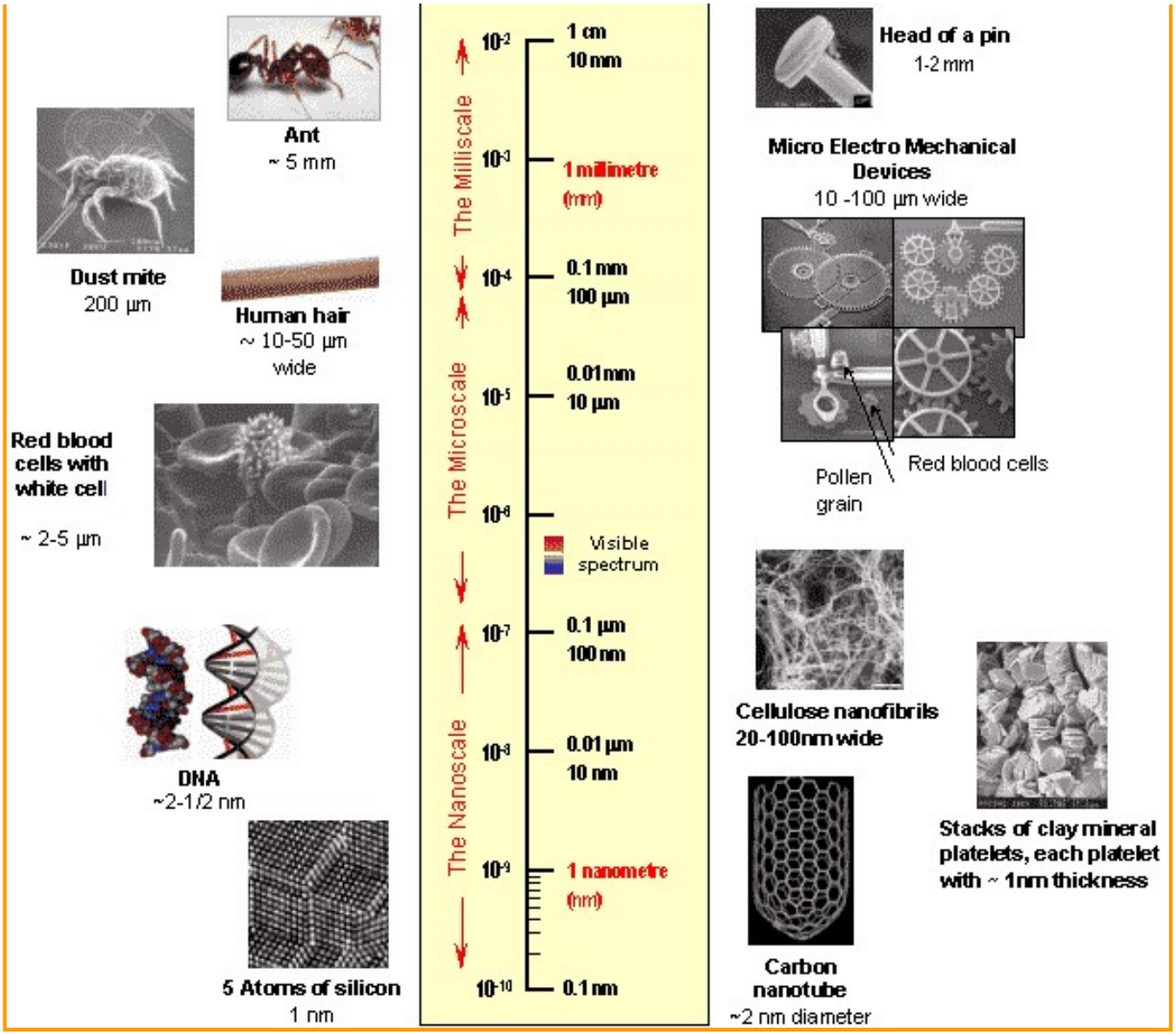
Faculty of Medicine, Charles University

and Czech Technical University

Prague, Czech Republic

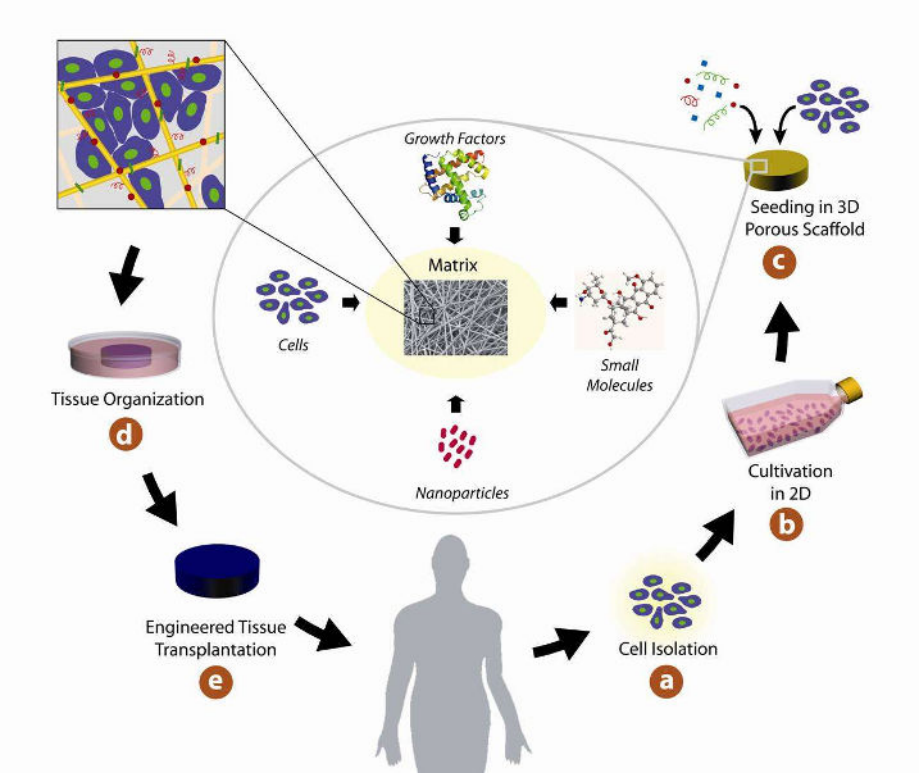
Group introduction

- Interests:
  - Smart regenerative medicine
  - Ultrasensitive detection
  - Controlled drug delivery and theragnostics
- Why nanofibers and their advantages
- Why GYNOCARE


Ant
~ 5 mm
Dust mite
200 µm
Human hair
~ 10-50 µm
wide
Red blood
cells with
white cell
~ 2-5 µm
DNA
~2-1/2 nm
5 Atoms of silicon
1 nm
The Milliscale
The Microscale
The Nanoscale
10-2
1 cm
10 mm
10-3
1 millimetre
(mm)
10-4
0.1 mm
100 µm
10-5
0.01mm
10 µm
10-6
Visible
spectrum
10-7
0.1 µm
100 nm
10-8
0.01 µm
10 nm
10-9
1 nanometre
(nm)
10-10
0.1 nm
Head of a pin
1-2 mm
Micro Electro Mechanical
Devices
10 -100 µm wide
Pollen
grain
Red blood cells
Cellulose nanofibrils
20-100nm wide
Stacks of clay mineral
platelets, each platelet
with ~ 1nm thickness
Carbon
nanotube
~2 nm diameter

Classical pathway of tissue engineering

Developement of tissue in *in vitro* conditions and implantation of fully functional implant with cells and ECM.



Plos:

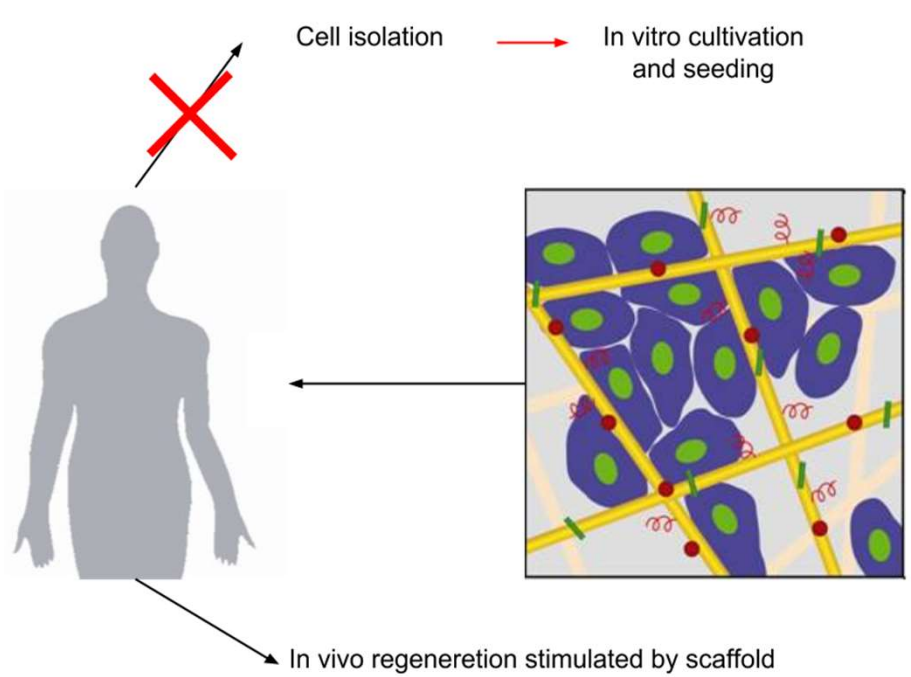
- Amplification of cells
- Control over cell differentiation
- Control over implant properties

Cons:

- Shock for cells in the stages of pathway
- Selection of fastes growing cells
- Nonphysiological stimulation
- Poor implant integration with surounding tissues

Modern pathway of regenerative medicine

Implantation of scaffolds and *in vivo* cell recrutiment and regeneration.

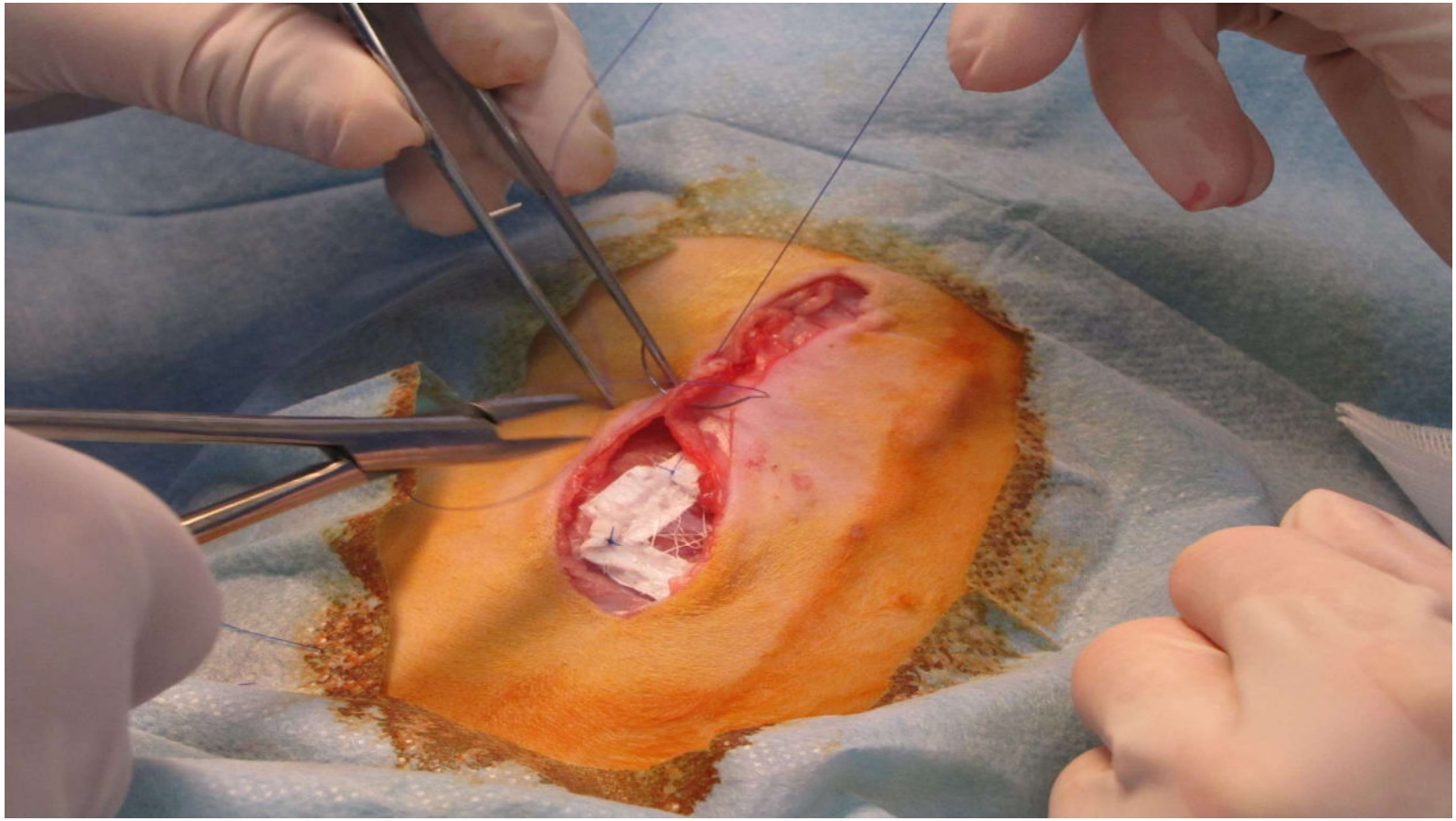


Plos:

- Limited danger of carcenogenesis
- Formation of complex tissues and better integration to surounding tissues
- Mimicking of natural healing

Cons:

- Complex scaffolding materials



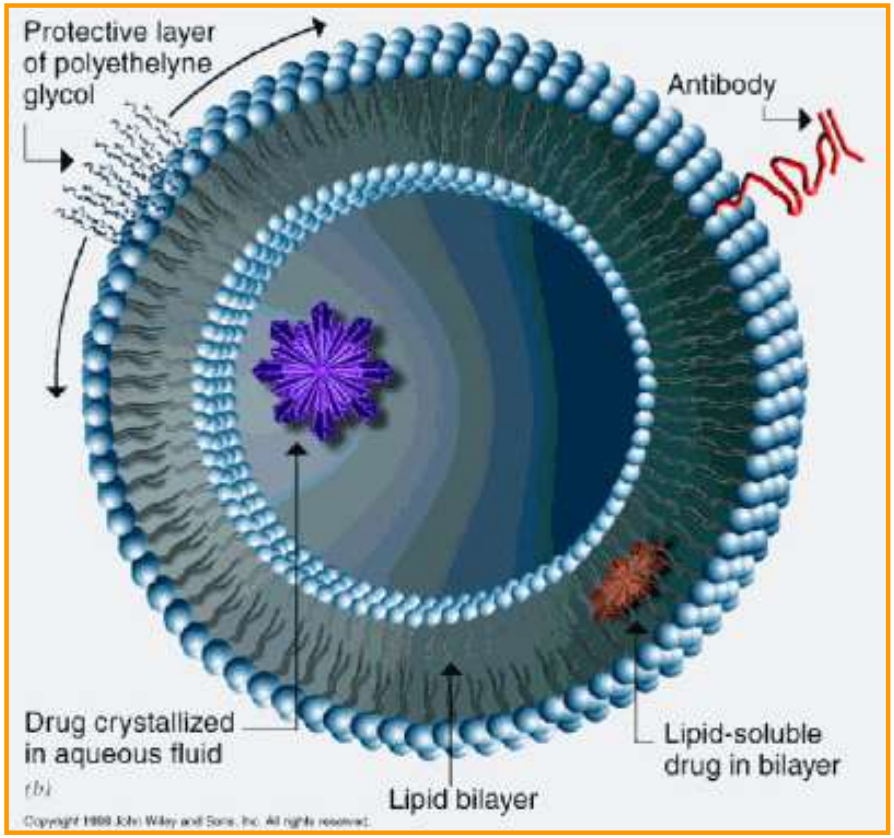
CONTROLLED DRUG DELIVERY

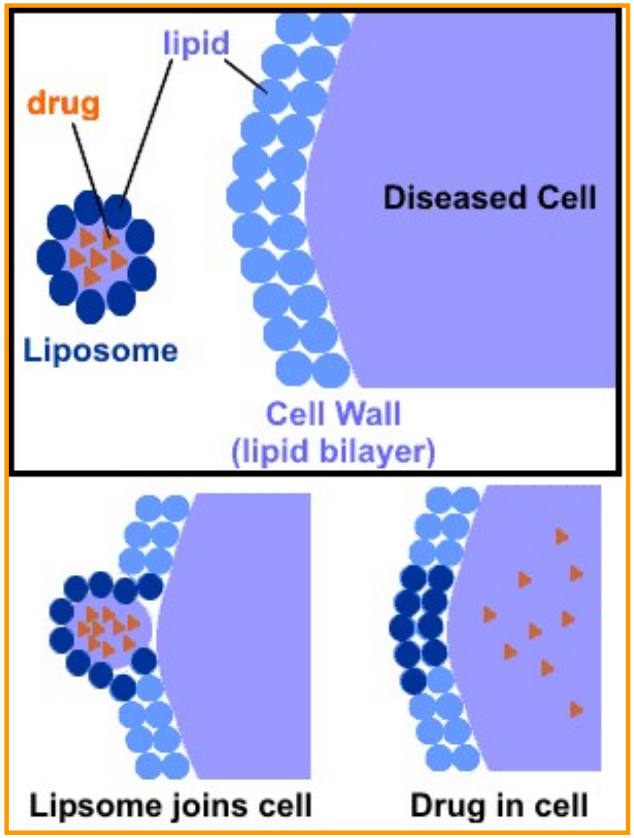
In controlled drug delivery, the drug is released over a period of time in a controlled manner. There is a concentration gradient in the target area. Physical quantity controlling the rate of the drug release is diffusion.

Drug carriers are substances facilitating time-controlled delivery, organ-specific targeting, protection, prolonged *in vivo* function, and decrease of toxicity of drugs.

Drug carriers: liposomes, albumine microparticles, soluble synthetic polymers, DNA complexes, conjugates protein-drug, erythrocyte-carriers, other biodegradable substances, …

Liposomes for drug delivery



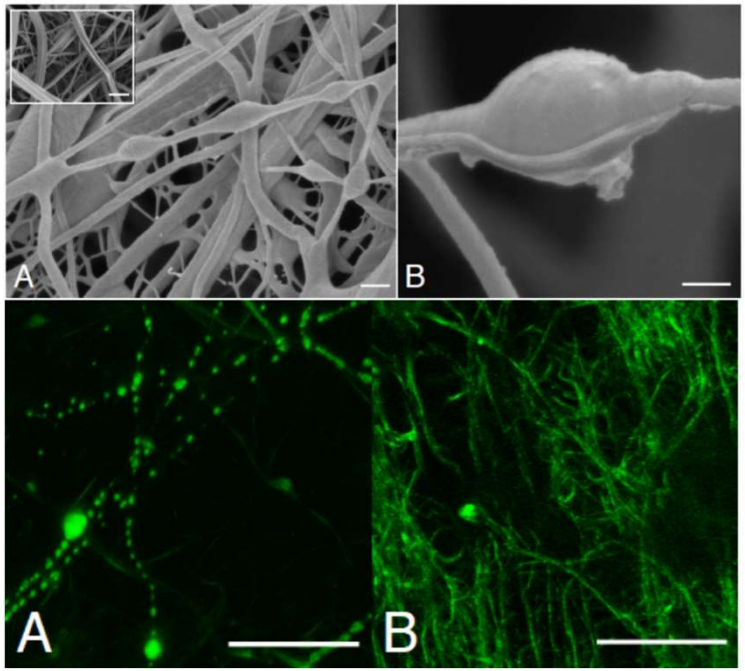


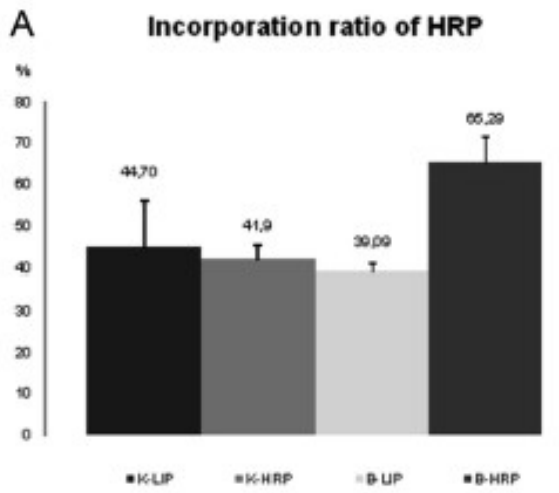
Core/shell nanofibers with embedded liposomes

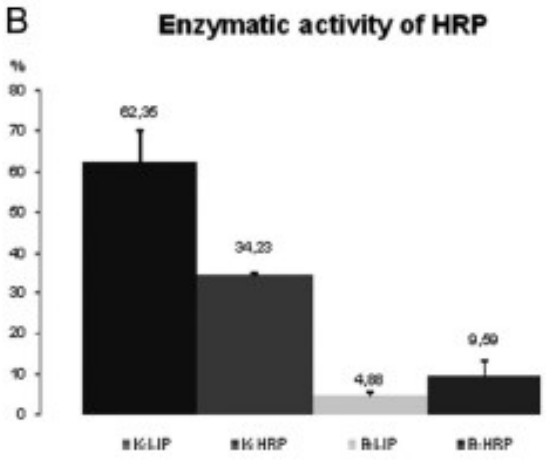
Nanofibers from PCL shell and PVA core with liposomes

PVA stabilize liposomes and they remain intact.

Activity of model enzyme significantly higher than with other methods.

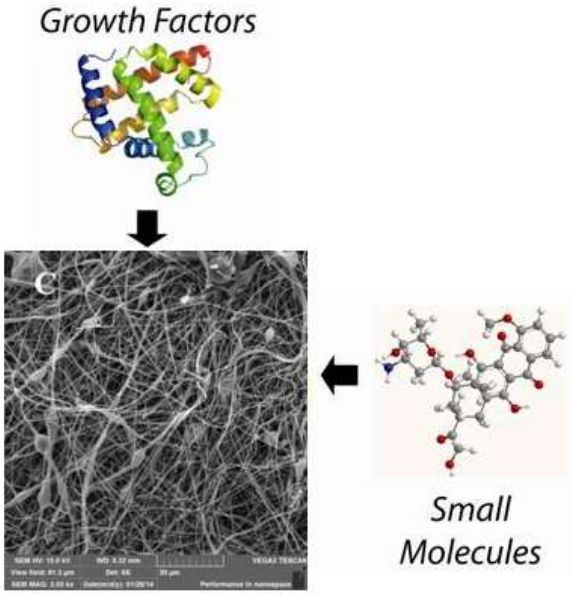


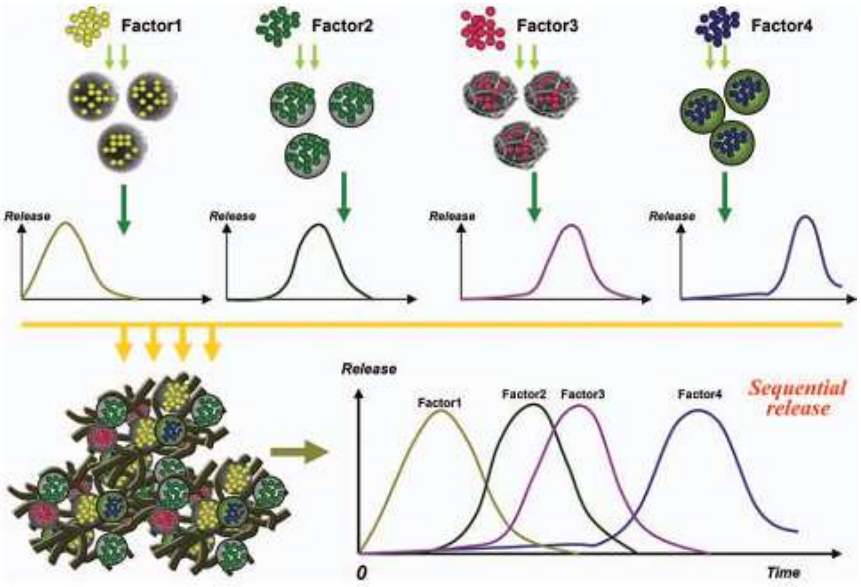




Advanced scaffold systems – drug delivery systems

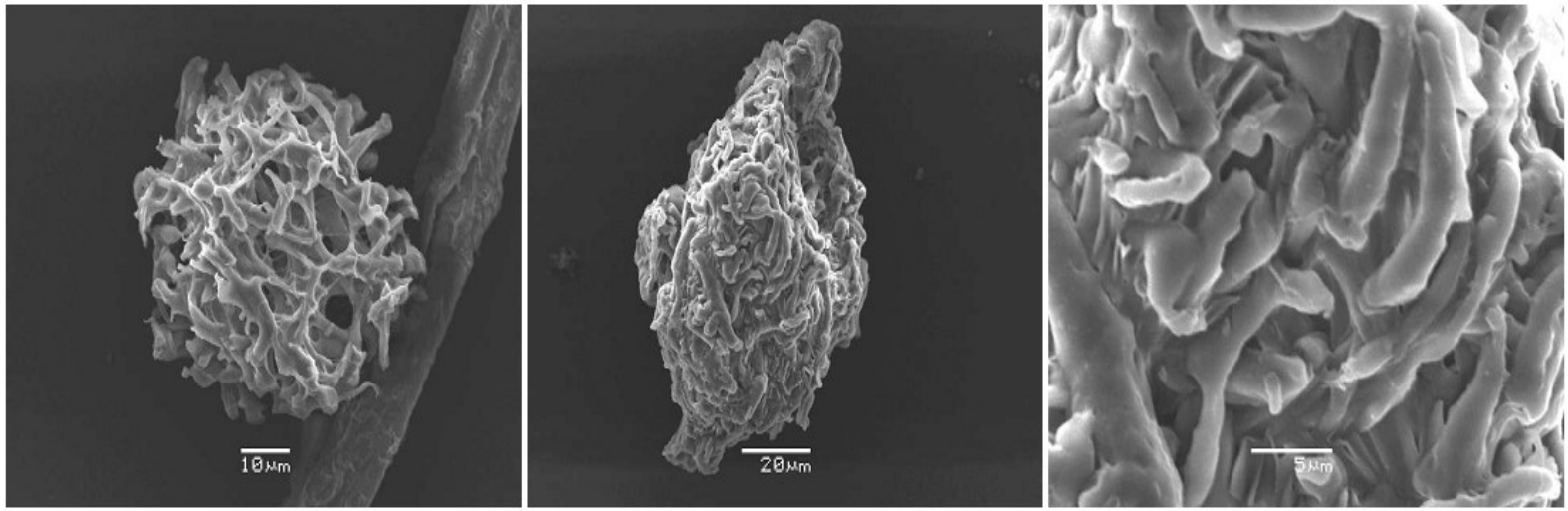
- For *in situ* regeneration advanced scaffold systems are necessary
- Scaffold must have:
  - Suitable chemical composition for promotion of regeneration
  - Mechanical properties respecting properties of tissue
  - Delivery of active molecules for stimulation of regeneration process



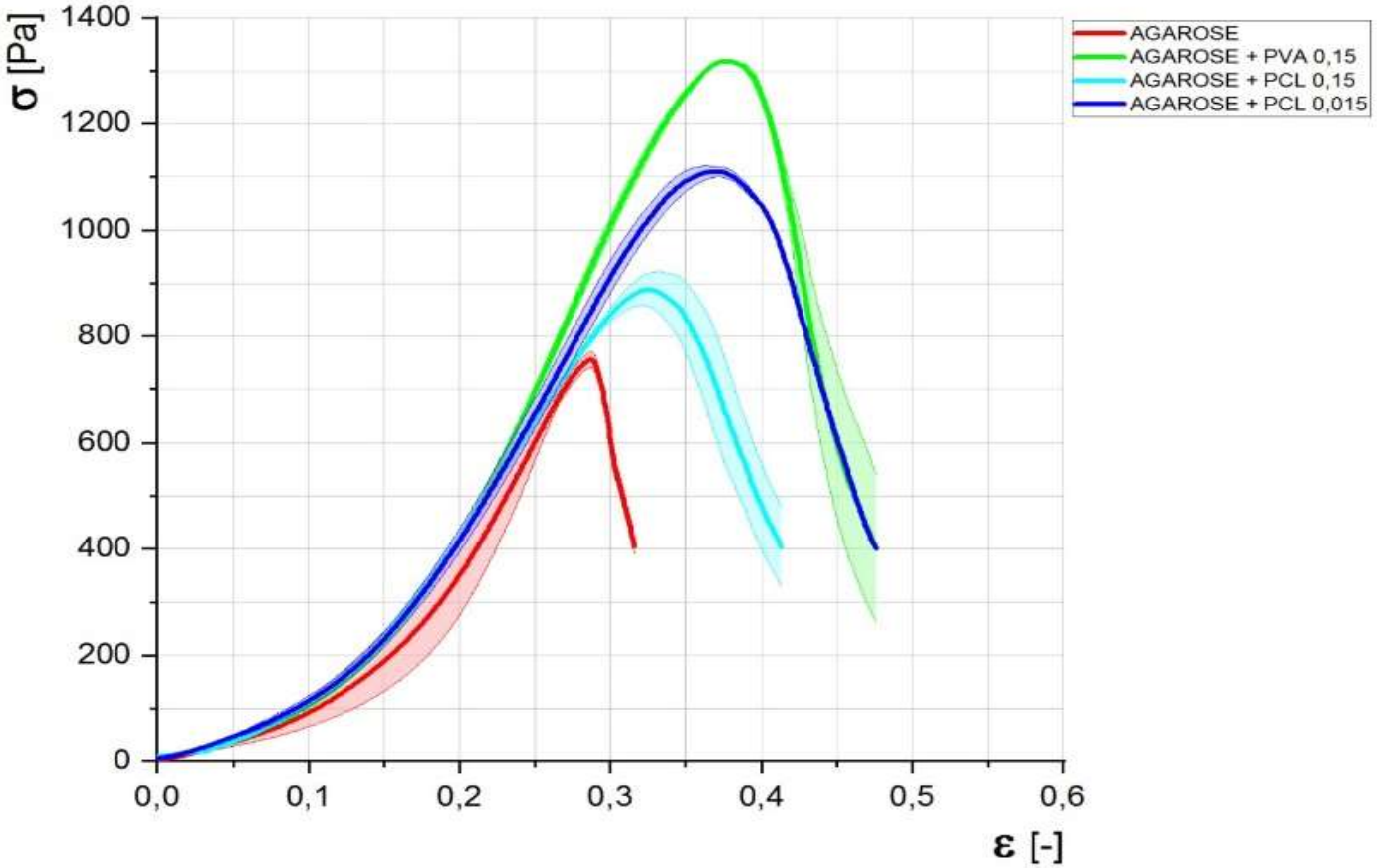


Fractionalized PCL nanofibers

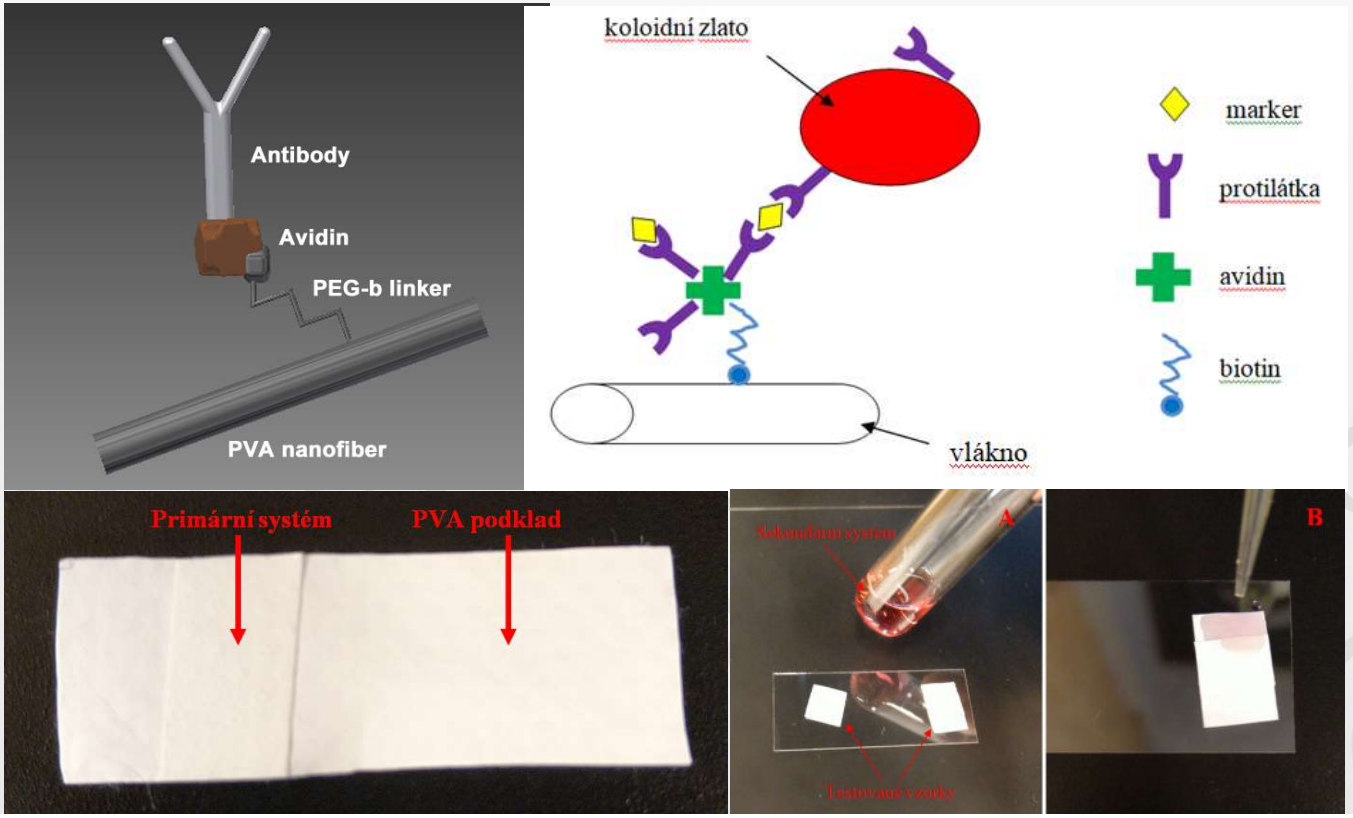
Cryogenic grinding is a facile technique for preparation of nanofiber derived microspheres.



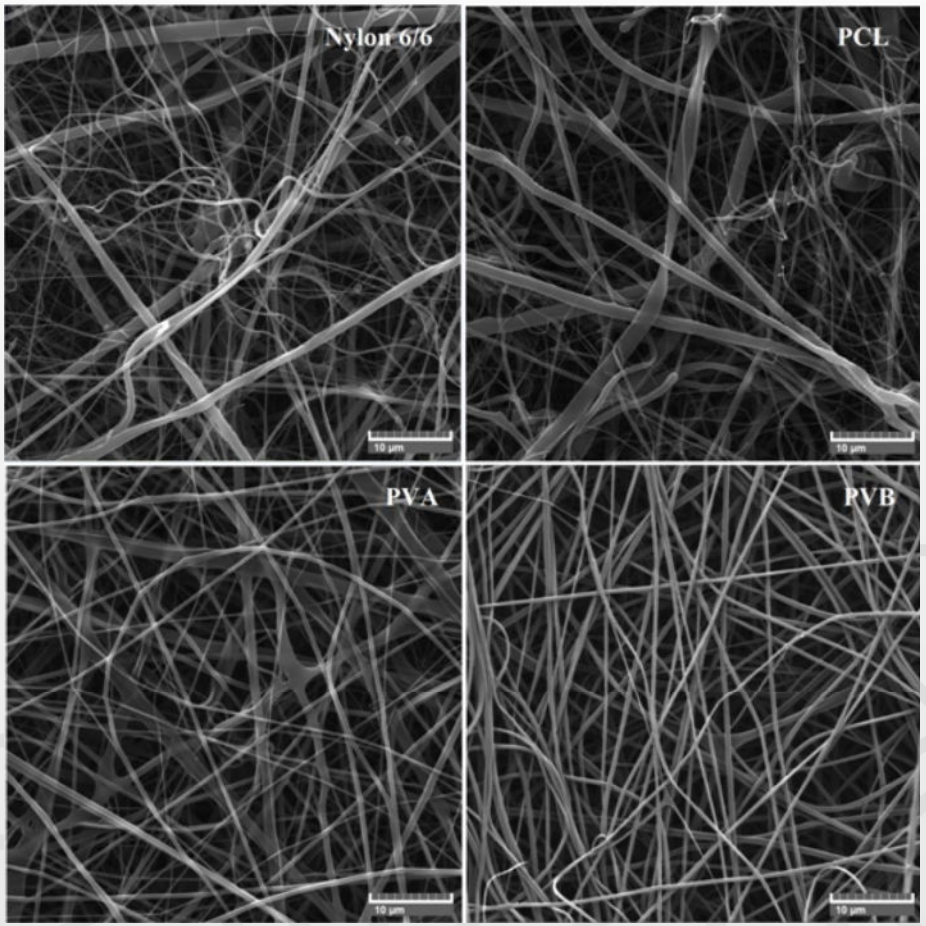
Modification of gel rigidity

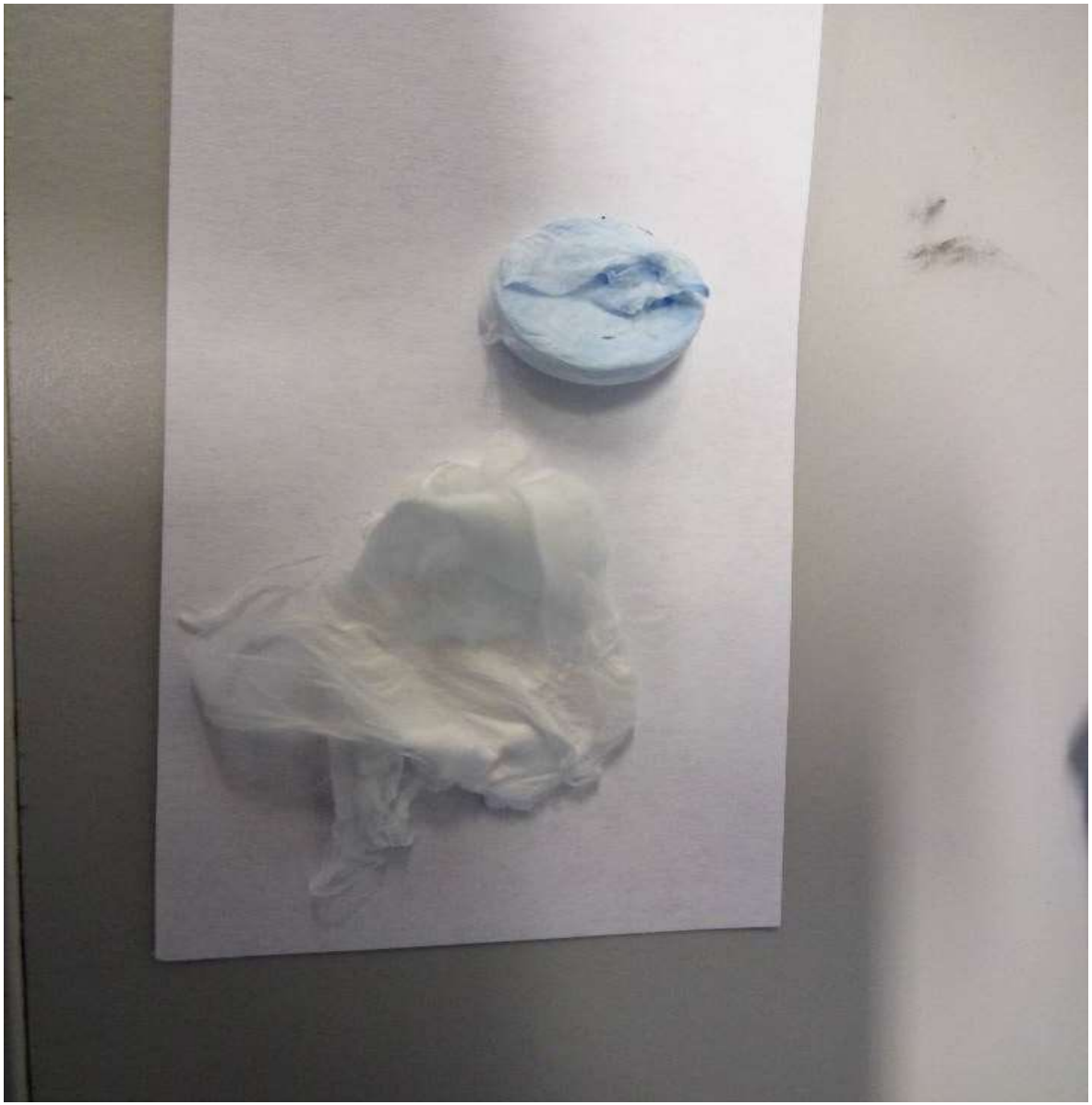


Specific biosensors



SEM analysis

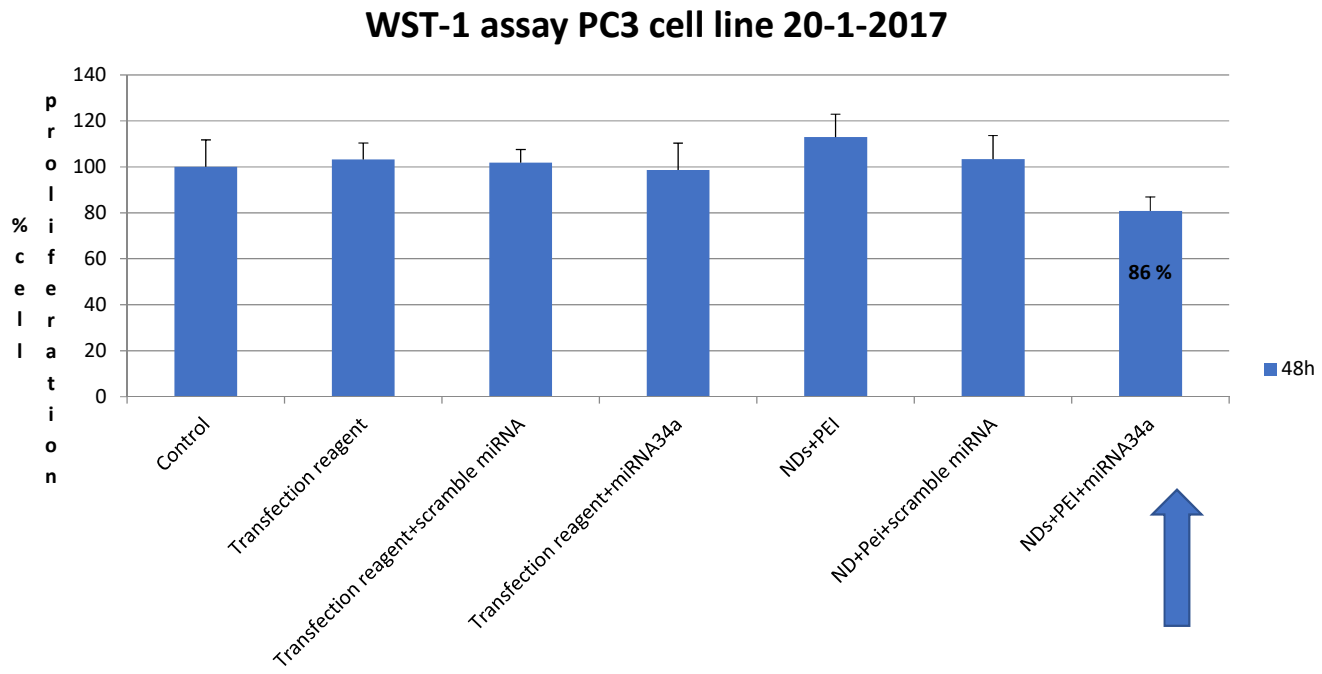




Why GYNOCARE?

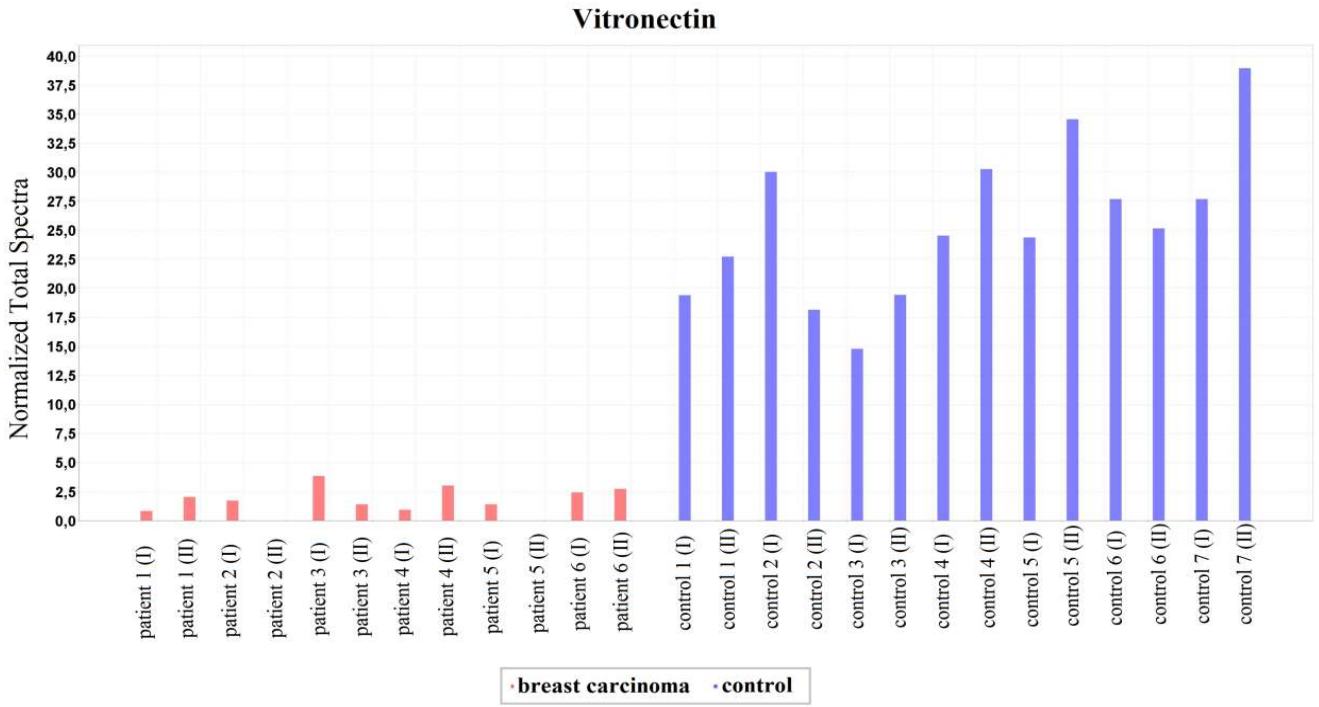
Looking for cooperation and specific nanofiber surface modification namely for ultrasensitive bionanosensors

PC3 cell line (prostatic cancer) proliferation assay

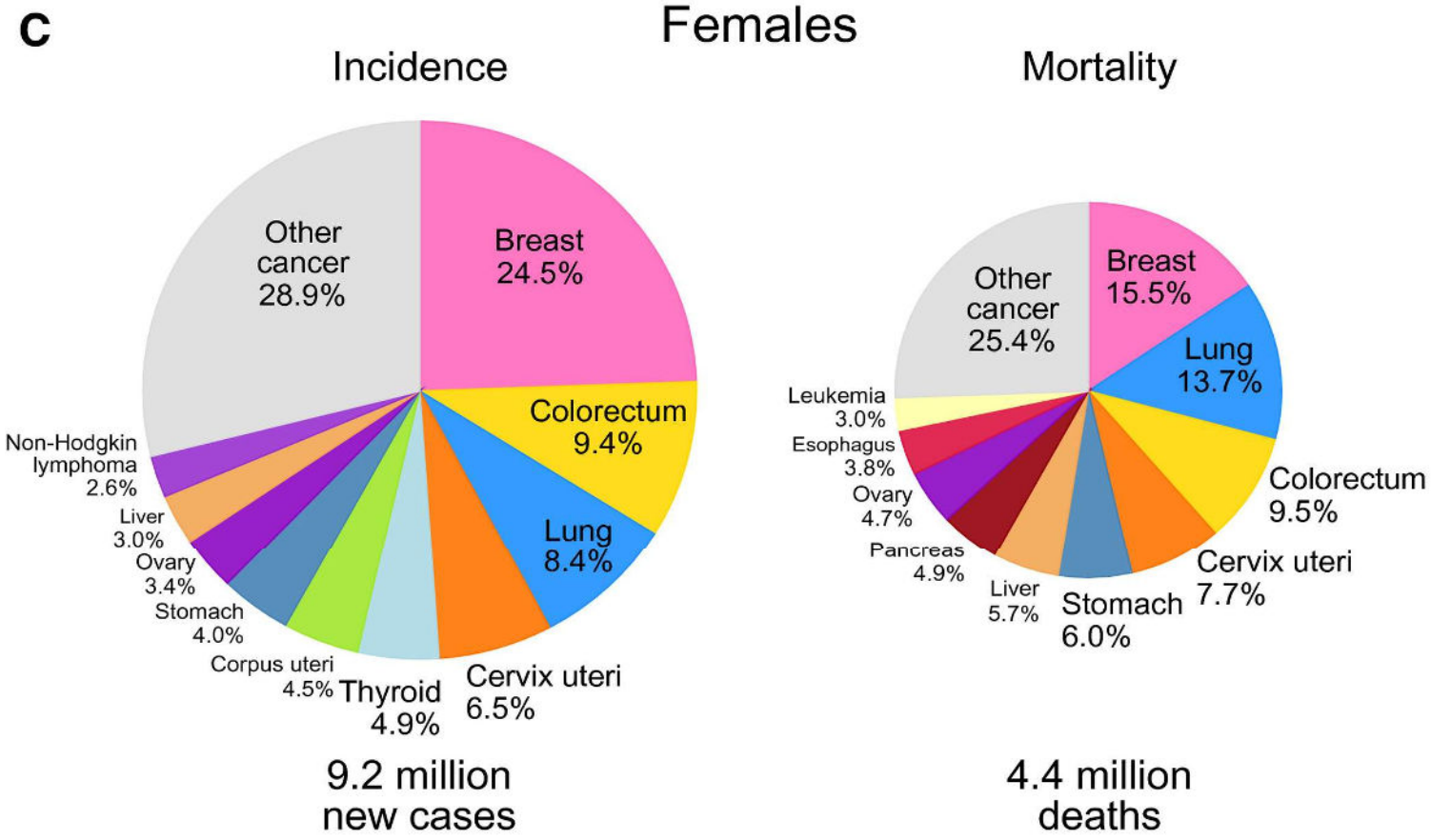


Reduced concentration of vitronectin in urine proteome in patients with breast carcinoma compared to control group

red – breast cancer patients
blue - control healthy group



Global Cancer Statistics 2020:
GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries



Multiple tumor marker tests on nanofibers

Colorectal	M2-PK; if M2-PK is not available, can test CEA, CA 19-9, CA 125
Breast	CEA, CA 15-3, Cyfra 21-1
Ovary	CEA, CA 19-9, CA 125, AFP, BHCG
Uterine	CEA, CA 19-9, CA 125, Cyfra 21-1, SCC
Prostate	PSA, FPSA and ratio
Testicle	AFP, BHCG
Pancreas/Stomach	CEA, CA 19-9, CA 72-4
Liver	CEA, AFP
Oesophagus	CEA, Cyfra 21-1
Thyroid	CEA, NSE
Lung	CEA, CA 19-9, CA 125, NSE, Cyfra 21-1 (Sensitivity at 95 percent percentile for Cyfra 21-1 is 79 percent, while for SCC and CEA are 41 and 31 percent respectively)[26]
Bladder	CEA, Cyfra 21-1, TPA

Potential biomarkers in the cervical vaginal fluid for the (self-)diagnosis of cervical precancer.

2018 , Van Ostade X, Dom M, Tjalma W, Van Raemdonck G

- Several DNA, DNA methylation, miRNA, and protein biomarkers were identified in the cervical vaginal fluid
- Proteins, especially alpha-actinin-4, are most suited for development of a simple assay for cervical (pre)cancer. Accuracy of the test could further be improved by combination of several proteins or by combination with a new type of biomarker, e.g., originating from the cervicovaginal microbiome or metabolome.

Gynecological biomarkers – exosomal miRNA

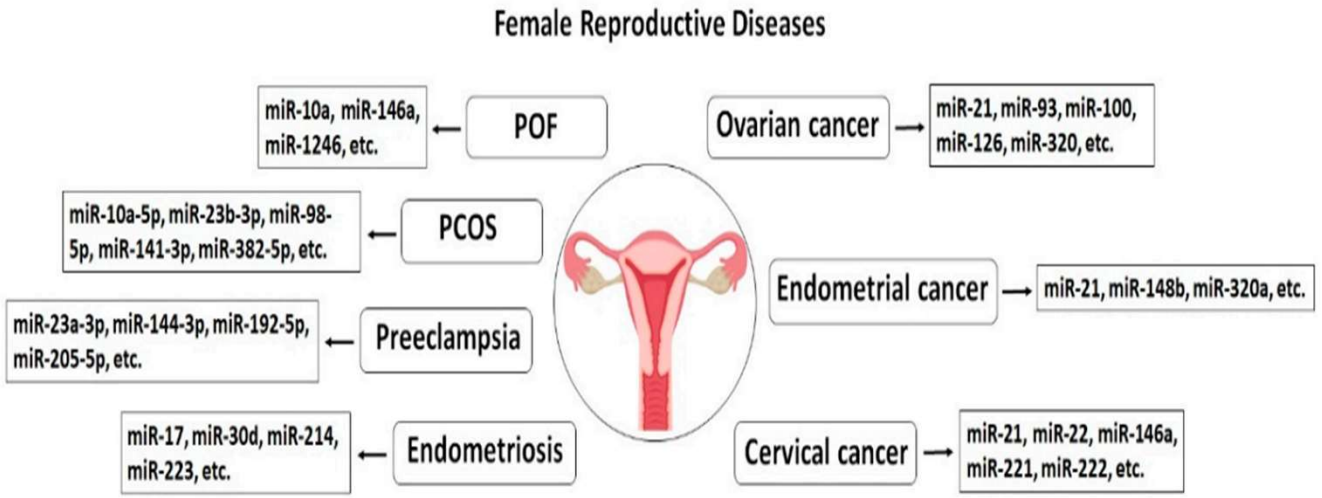


Figure 2. A summary of exosomal miRNAs reported in recent studies considering their role in the pathogenesis of the most noticeable female reproductive diseases. miR, miRNA, microRNA; POF; Premature Ovarian Failure, PCOS; Polycystic Ovary Syndrome.

- Exosomes as Biomarkers for Female Reproductive Diseases Diagnosis and Therapy. Int J Mol Sci. 2021
- Esfandyari S, Elkafas H, Chugh RM, Park HS, Navarro A, Al-Hendy A.

Theragnostic potential - miRNA

- Potential role of microRNAs in the treatment and diagnosis of cervical cancer. Cancer Genet. 2020

- Shen S, Zhang S, Liu P, Wang J, Du H.

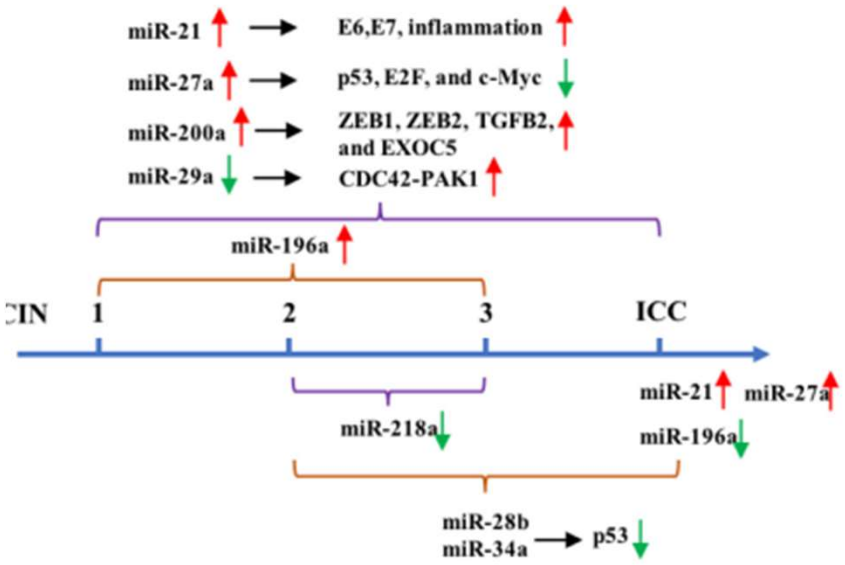


Fig. 1 Aberrant miRNA expressions in cervical cancer.

GYNOCARE

European network for Gynaecological Rare Cancer research: From Concept to Cure

Thank you for your attention

Grazzi ta' l-attenzjoni

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Website: www.gynocare.net