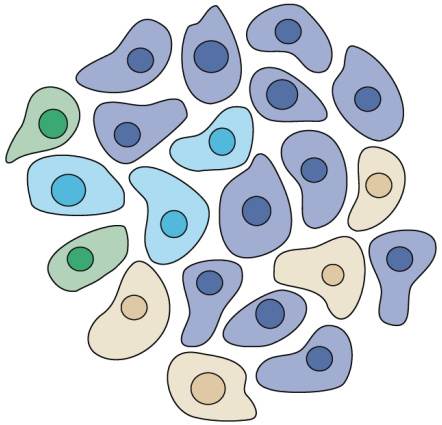
Speciální metody FŽ

METODY STUDIA BUNĚČNÉ PLASTICITY A NÁDOROVÉ PROGRESE



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IBP
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AZV ČR
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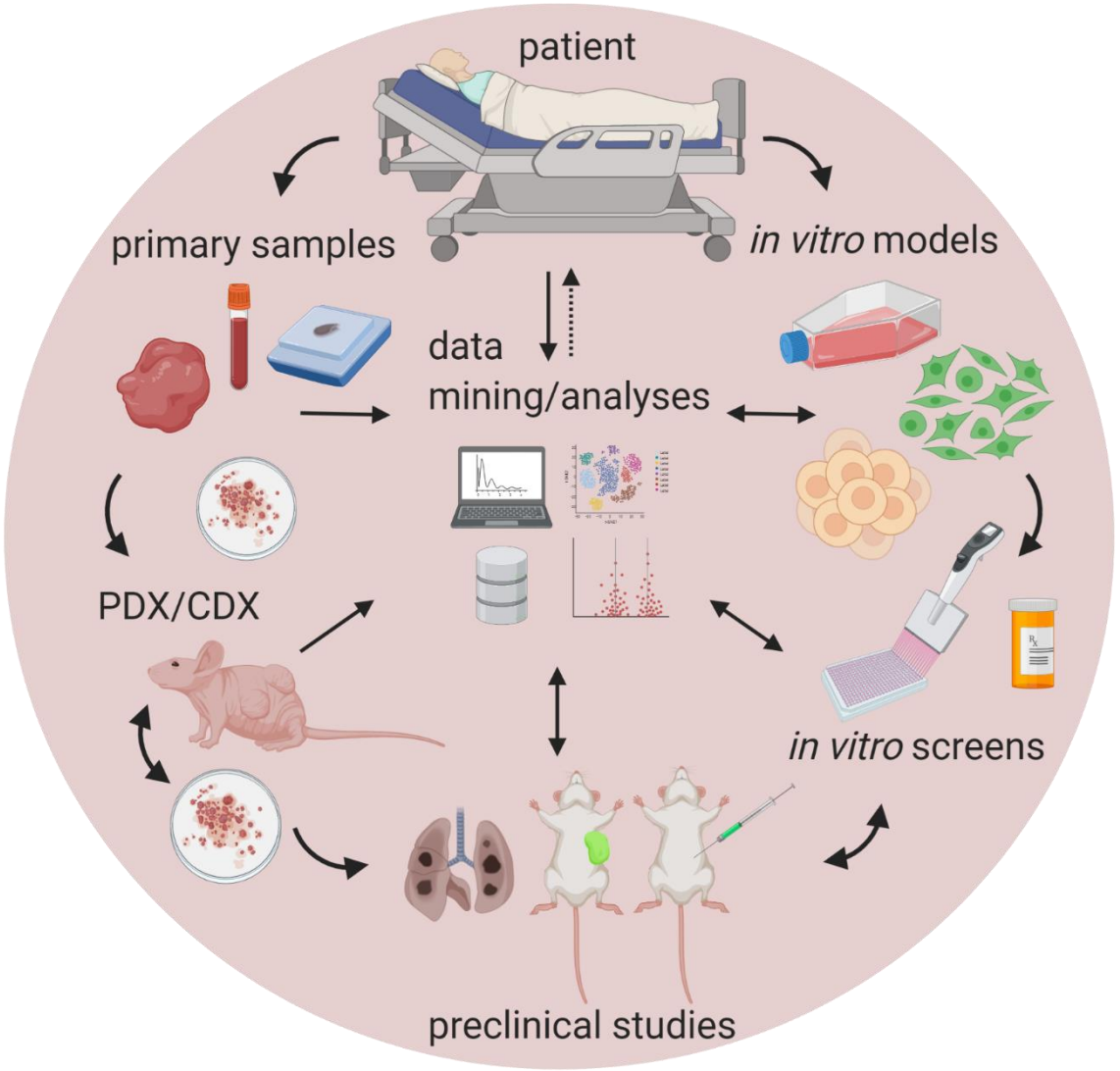
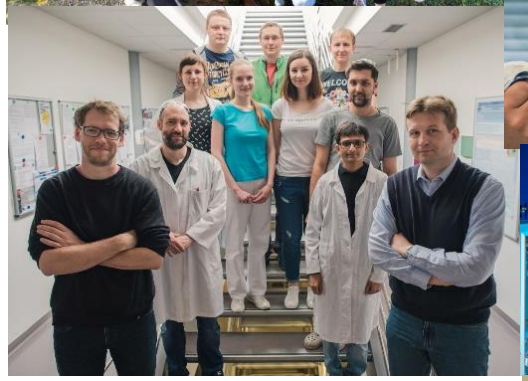


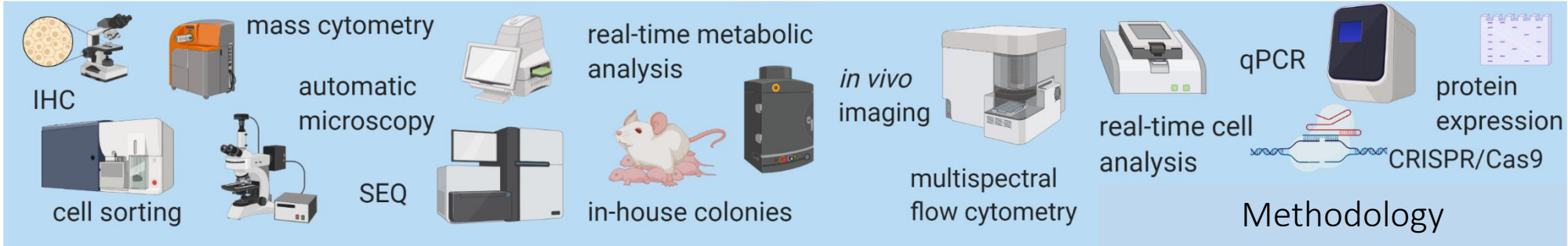
Team & Collaborators







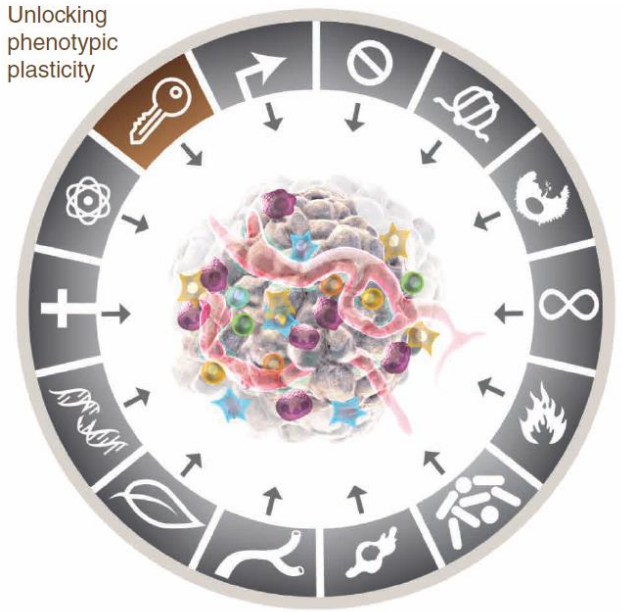



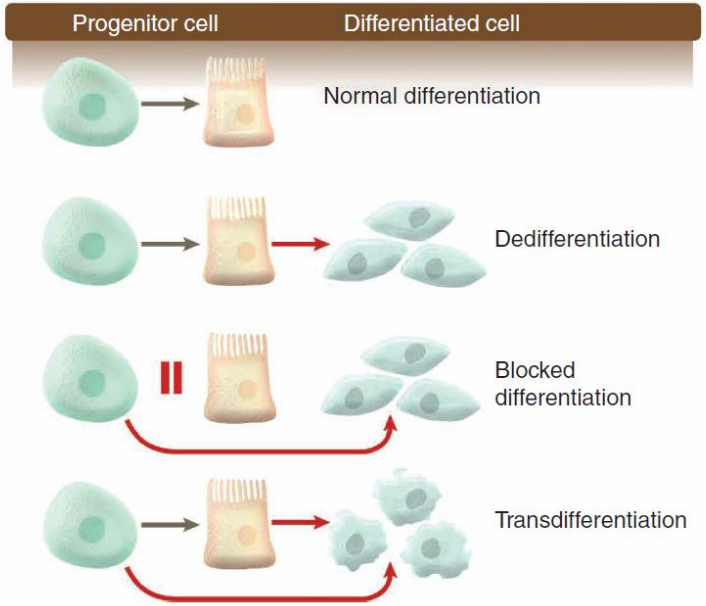
Otázky

- Jak studujeme vlastnosti nádorových buněk – migraci, invazivitu *in vitro* a *in vivo*?
- Jak hodnotíme plasticitu fenotypu (nejen) nádorových buněk?
- Proč má smysl studovat nádorové cirkulující buňky a proč to vůbec není snadné?
- Jaká je role buněčného fyziologa/biologa v translačním/preklinickém výzkumu?
- Jak lze studovat mechanismy plasticity z pohledu regulace a funkce?

Typické znaky nádorové buňky

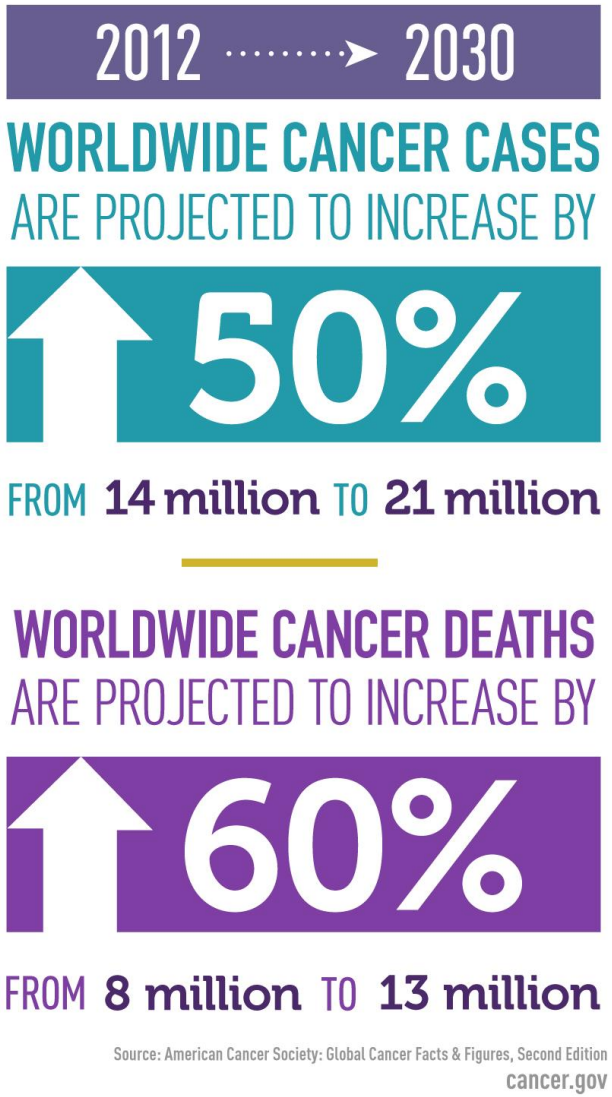
- podpůrné proliferační signály
- deregulace supresorů růstu/proliferace
- odolnost k buněčné smrti
- neomezená replikace
- neoangiogeneze
- invaze a metastázování
- mutace a genomická nestabilita
- zánět
- přestavba energetického metabolismu
- únik před zničením imunitním systémem
- Senescence*
- Plasticita*
- Epigenetika*
- Mikrobiom*



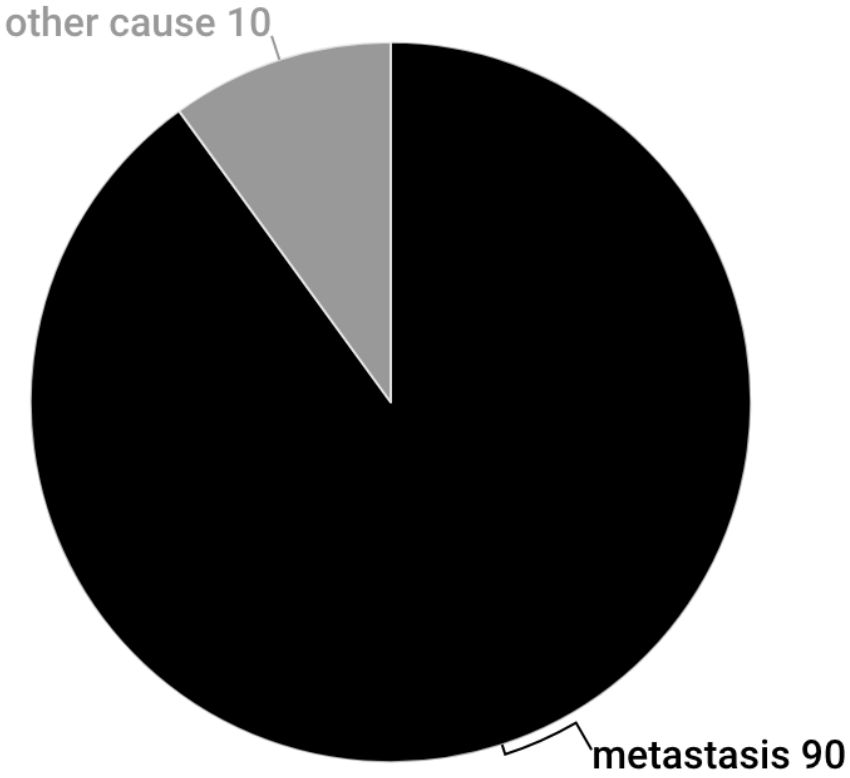


Douglas Hanahan & Robert A. Weinberg: Hallmarks of Cancer: Next Generation, Cell, 2011
*Hanahan, 2022

Why is cancer so devastating?

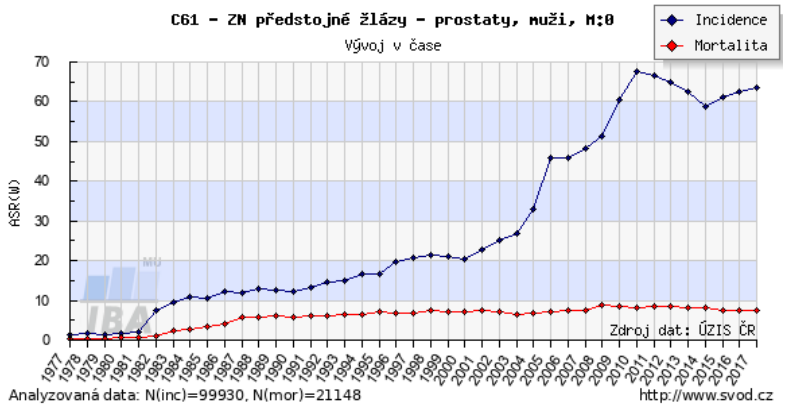


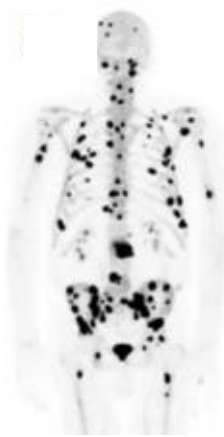
cancer-related death cause estimate

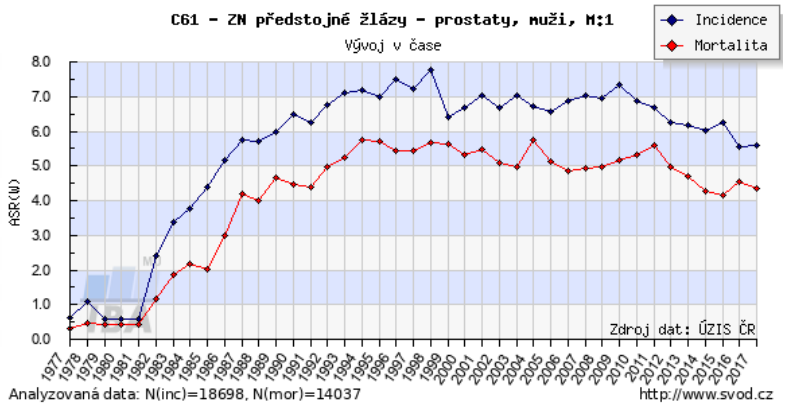


Why is cancer so devastating?

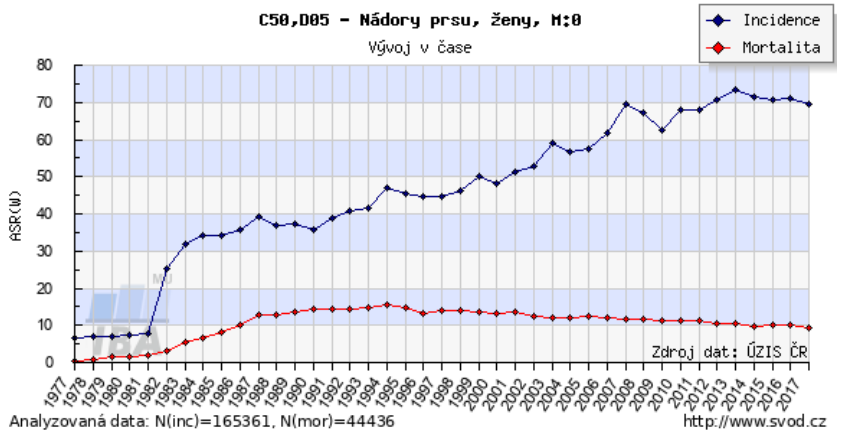
Prostate cancer

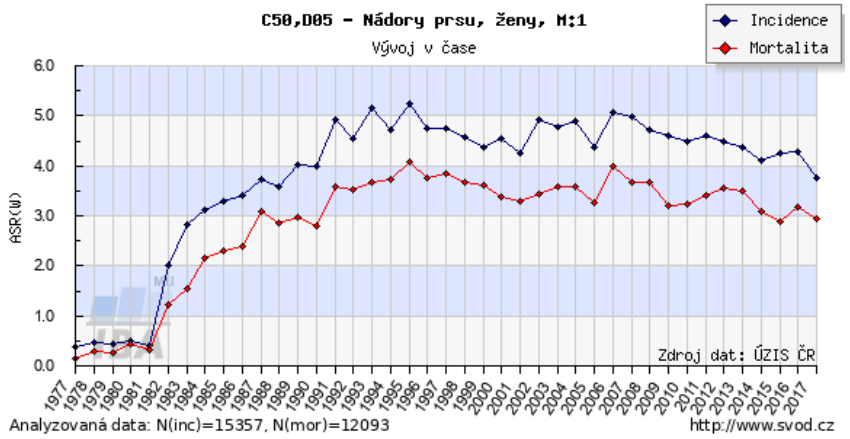






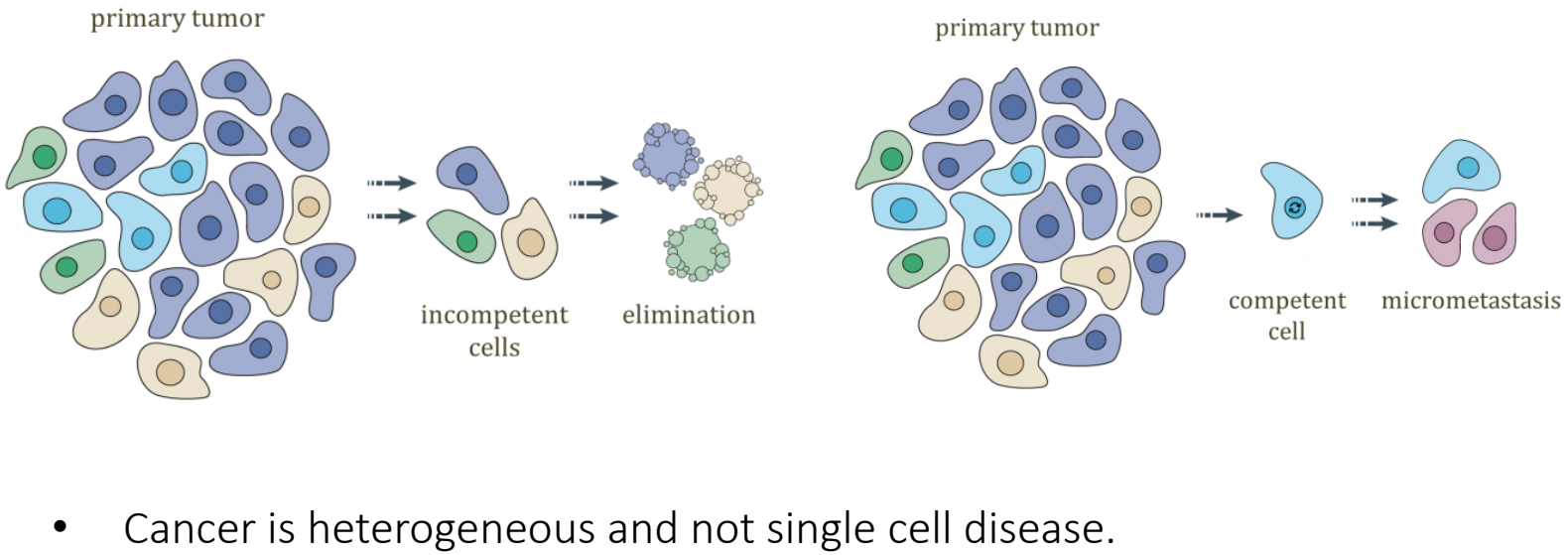
Breast cancer





Overview of current research

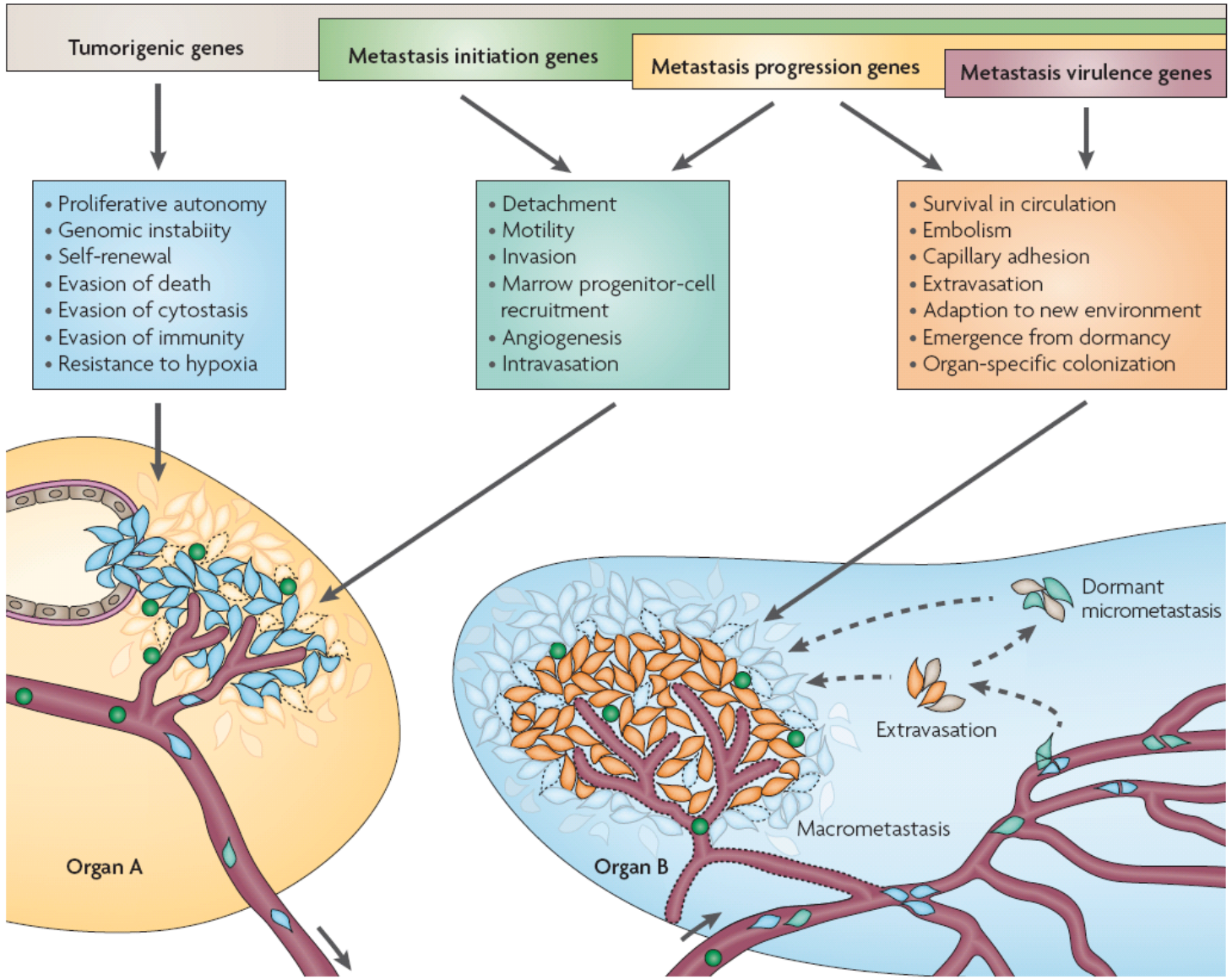
What kind of cells drives metastasis and how we can target them?



- Cancer is heterogeneous and not single cell disease.
- Complex and dynamic, NOT static “ecosystem”.
- Diversity inside tumors is clinical problem limiting the efficacy of targeted therapies and compromising treatment outcomes
- 90% of cancer related deaths are due to metastasis

Genetic determinants of cancer metastasis

Don X. Nguyen and Joan Massagué



Epithelial-Mesenchymal Transition (EMT)

- Změna buněčného fenotypu spojená se ztrátou adheze a zvýšením motility

Table 14.1 Examples of EMTs during mouse embryonic development

Process	Transition	
	From	To
Gastrulation	epiblast	mesoderm
Prevalvular mesenchyme in the heart	endothelium	atrial and ventricular septum
Neural crest cells	neural plate	neural crest cells, which can yield bone, muscle, peripheral nervous system
Somitogenesis	somite walls	sclerotome
Palate formation	oral epithelium	mesenchymal cells
Müllerian duct regression	Müllerian tract	mesenchymal cells

Adapted from P. Savagner, *BioEssays* 23:912–923, 2001.

EMT & nádory

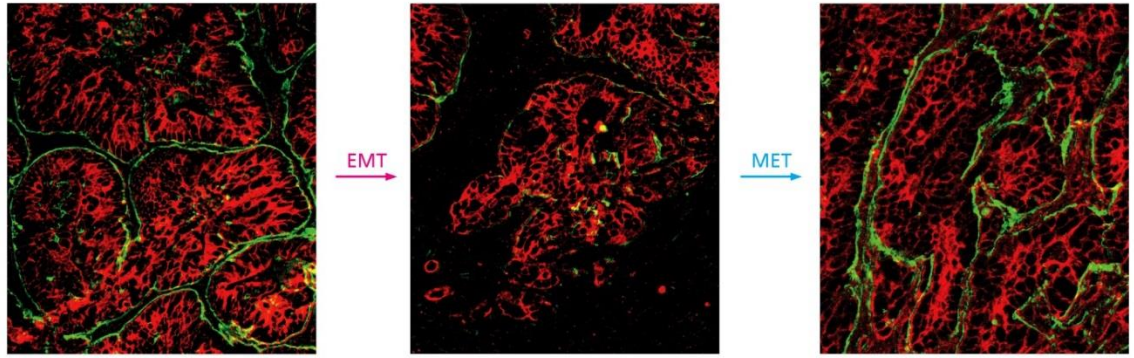


Figure 14.18a The Biology of Cancer (© Garland Science 2014)

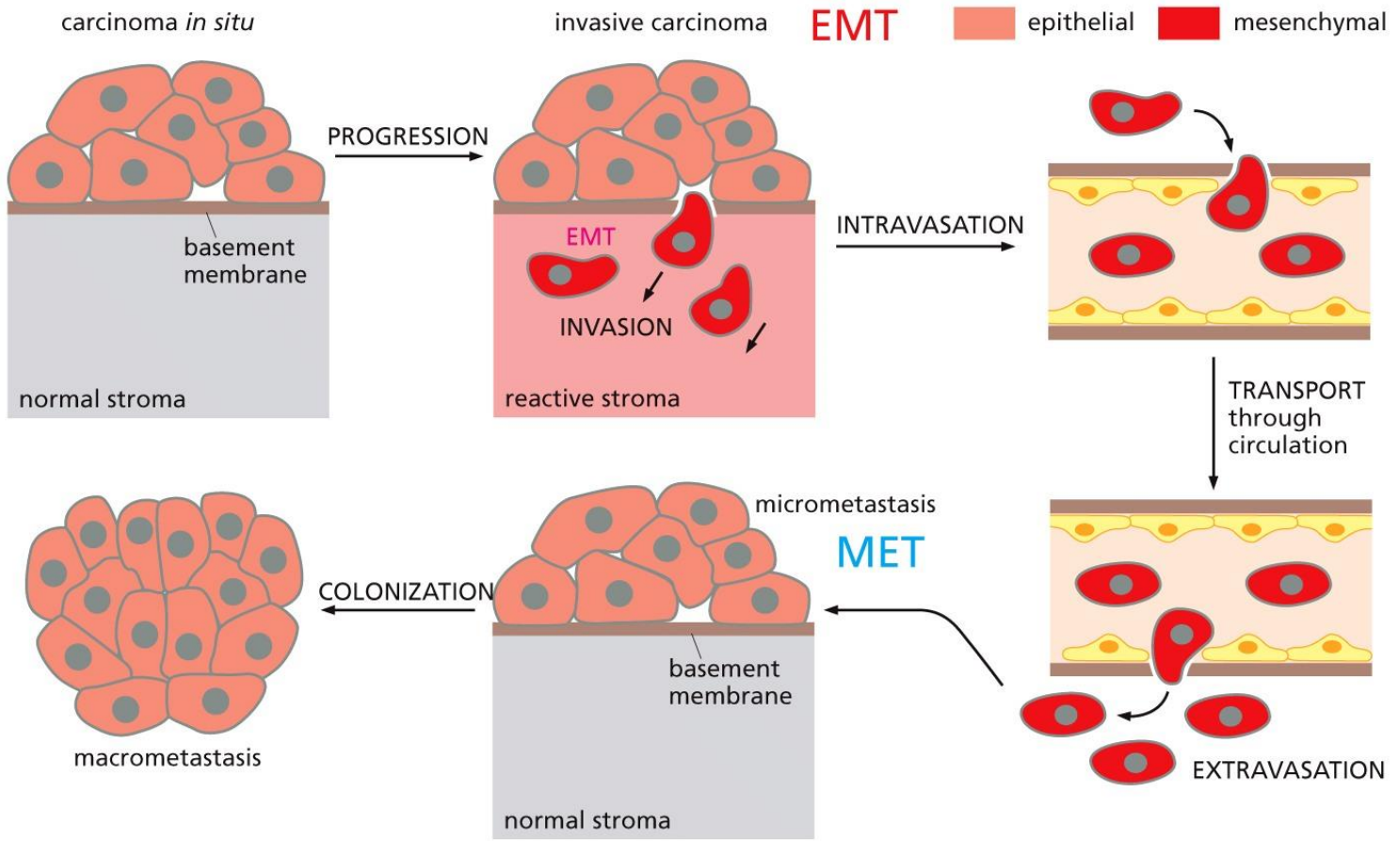


Figure 14.18b The Biology of Cancer (© Garland Science 2014)

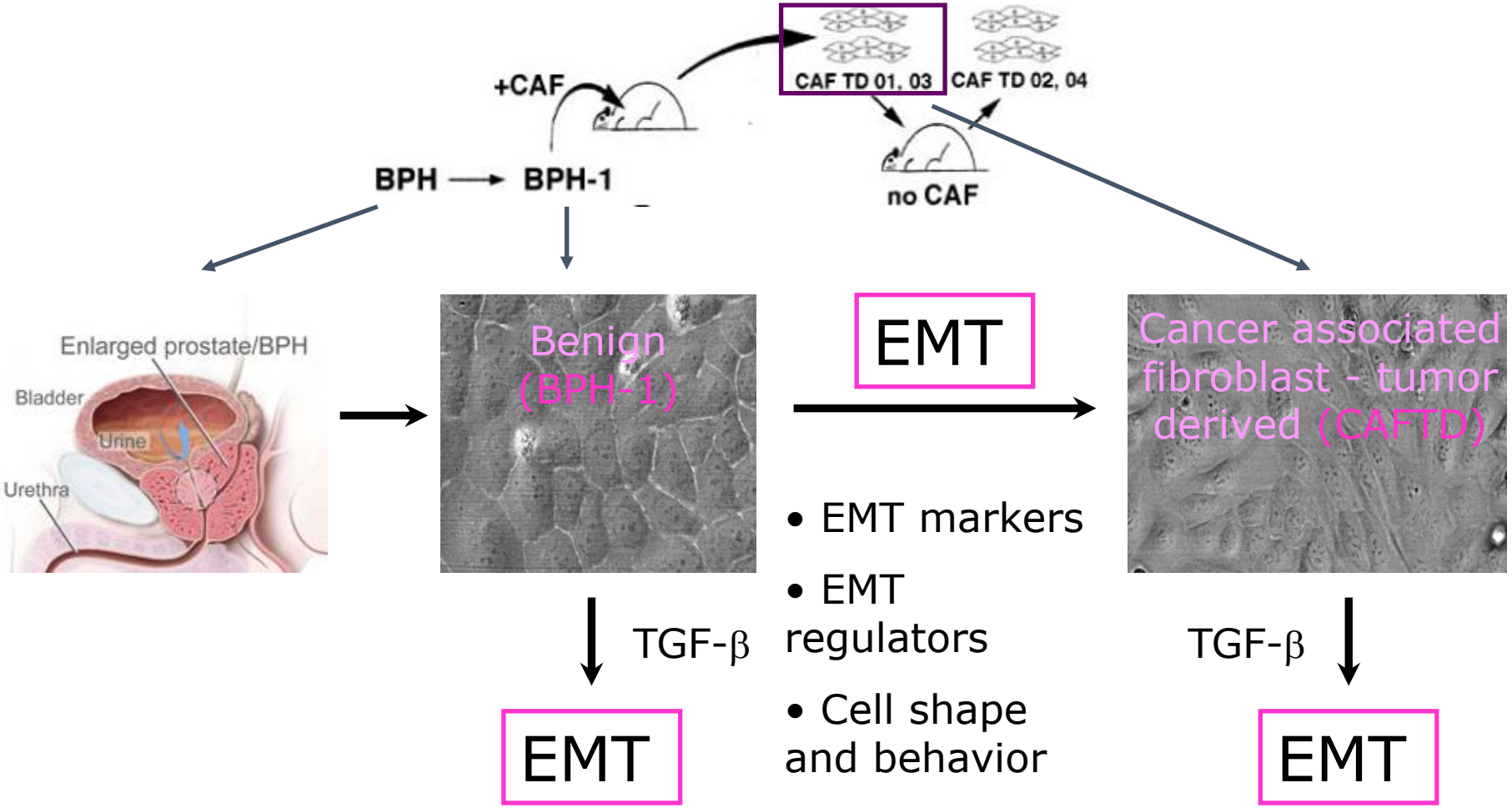
Experimentální přístupy

ESTABLISHMENT AND CHARACTERIZATION OF AN IMMORTALIZED BUT NON-TRANSFORMED HUMAN PROSTATE EPITHELIAL CELL LINE: BPH-1

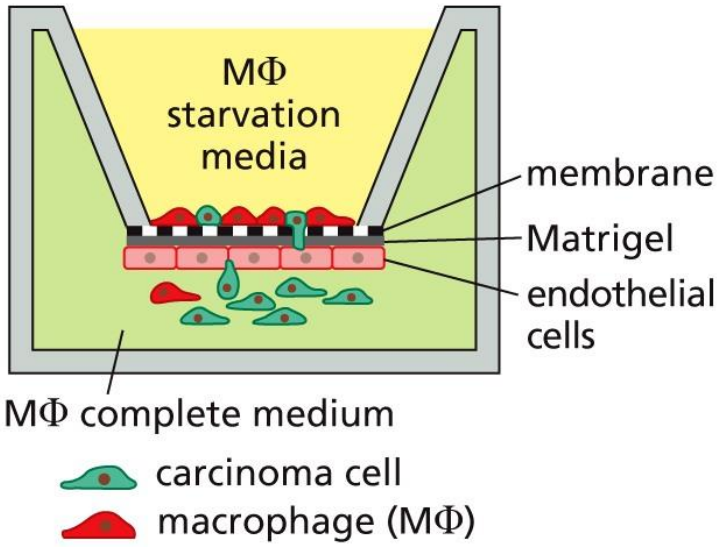
S. W. HAYWARD, R. DAHIYA, G. R. CUNHA, J. BARTEK, N. DESHPANDE, AND P. NARAYAN

Malignant Transformation in a Nontumorigenic Human Prostatic Epithelial Cell Line[1]

Simon W. Hayward,[2] Yuzhuo Wang, Mei Cao, Yun Kit Hom, Baohui Zhang, Gary D. Grossfeld, Daniel Sudilovsky, and Gerald R. Cunha



Analýza migračního potenciálu *in vitro*



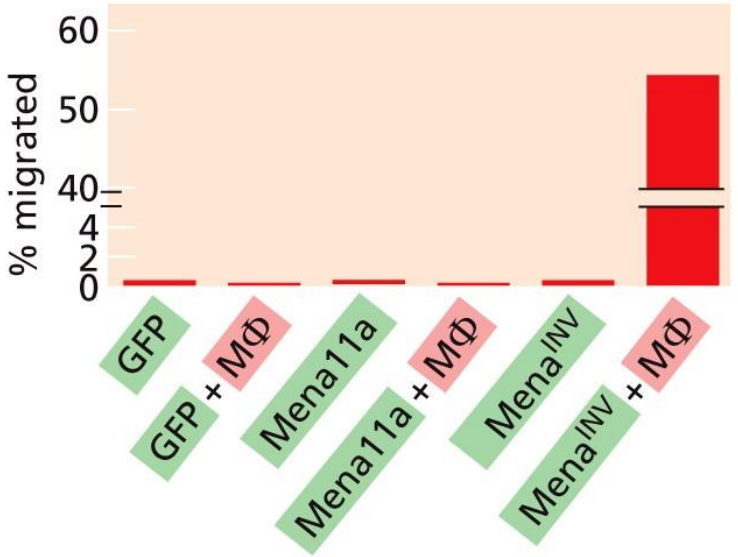
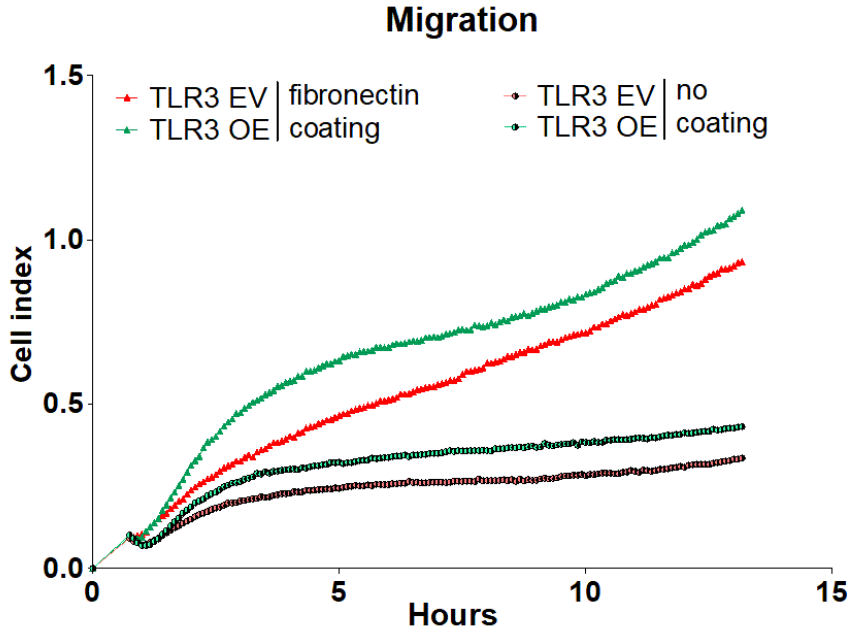
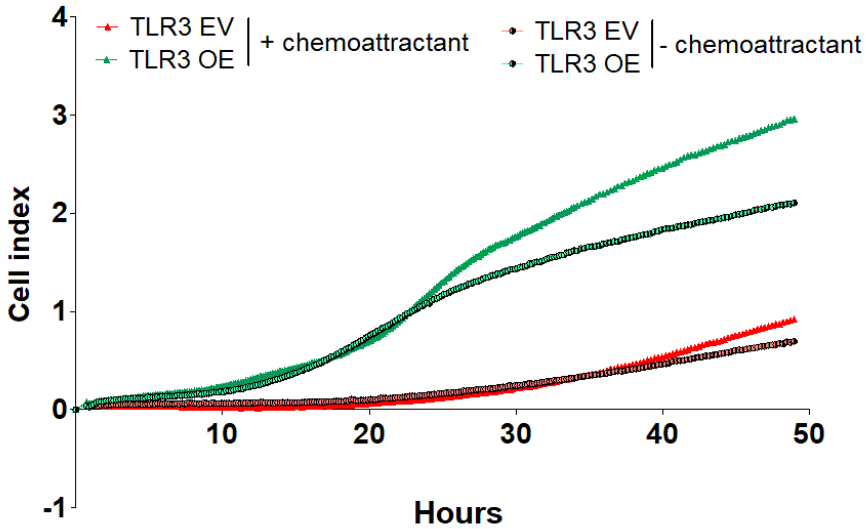


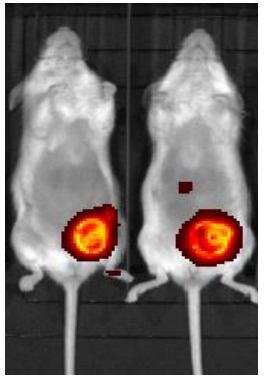
Figure 14.41c The Biology of Cancer (© Garland Science 2014)



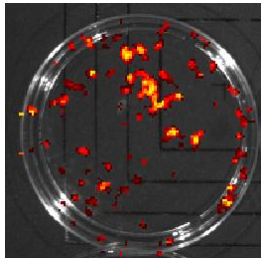


Analýza nádorové progrese *in vivo*

MDAMB-231
Human breast cancer

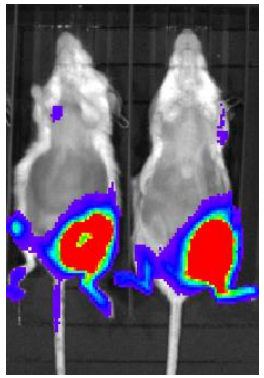


Mammary fat pad injection

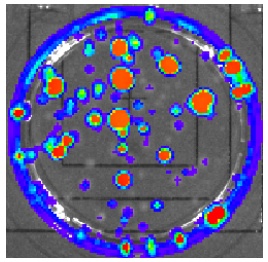


CTCs

4T1 12B
Murine mammary gland cancer

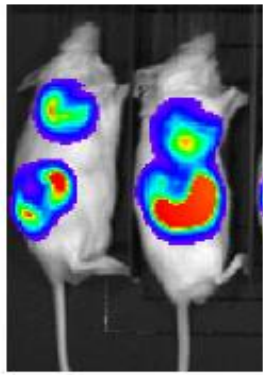


Mammary fat pad injection

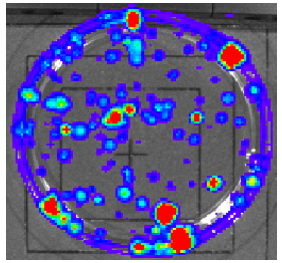


CTCs

A375 IV
Human melanoma

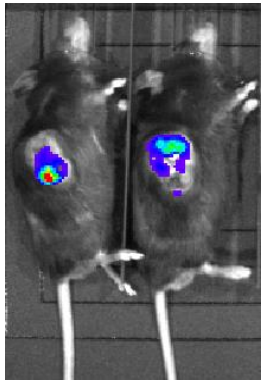


Intradermal injection



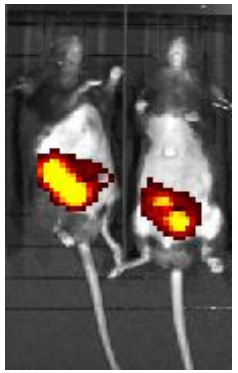
CTCs

Yumm 5.2
Murine melanoma

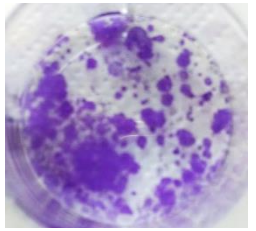


Intradermal injection

RM1
Murine prostate cancer

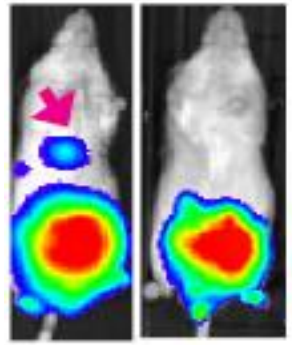


Intraprostate injection



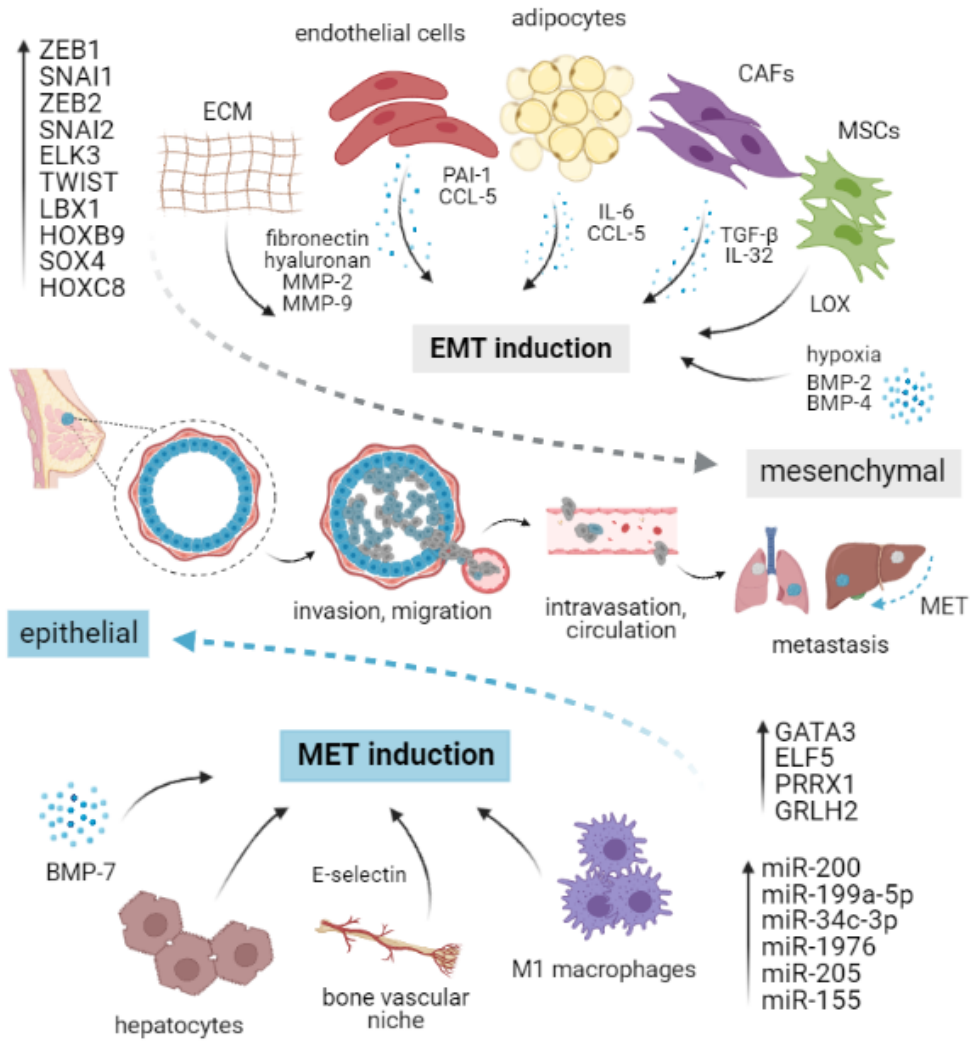
CTCs

DU145
Human prostate cancer



Intraprostate injection

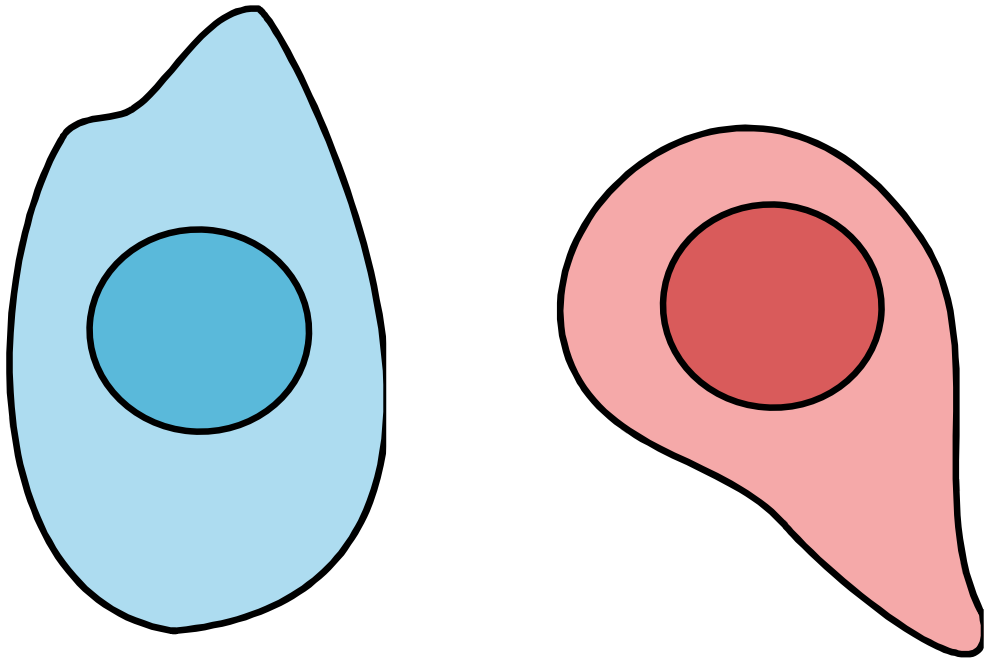
EMT/MET plasticity in cancer



B. Kvokačková,et al., *Cancers*, 2021

SOUČEK lab

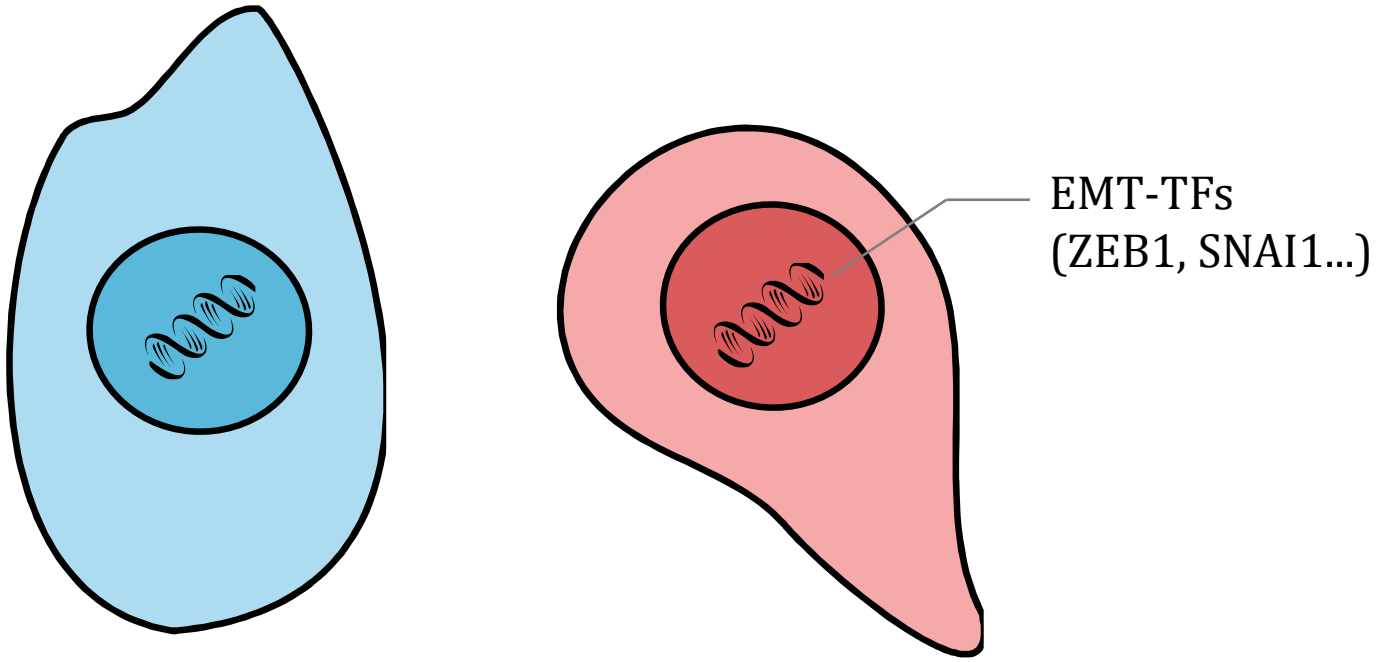
EMT and regulation of cell surface phenotype



EMT drives phenotypic diversity of the tumor
through the regulation of transcriptome

SOUČEK lab

EMT and regulation of cell surface phenotype



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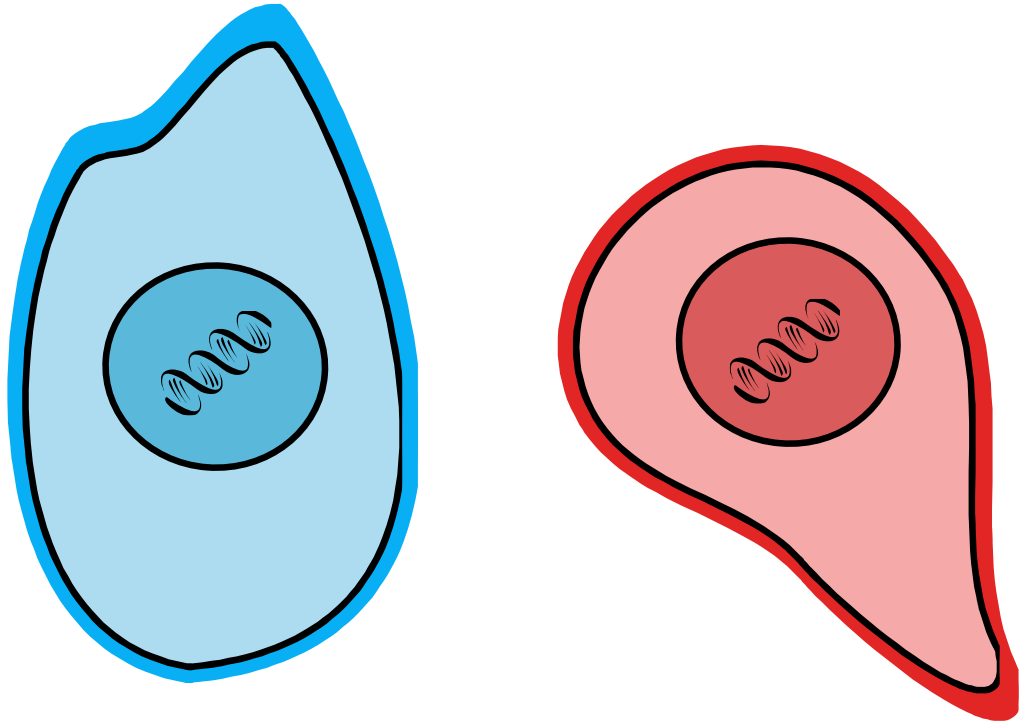
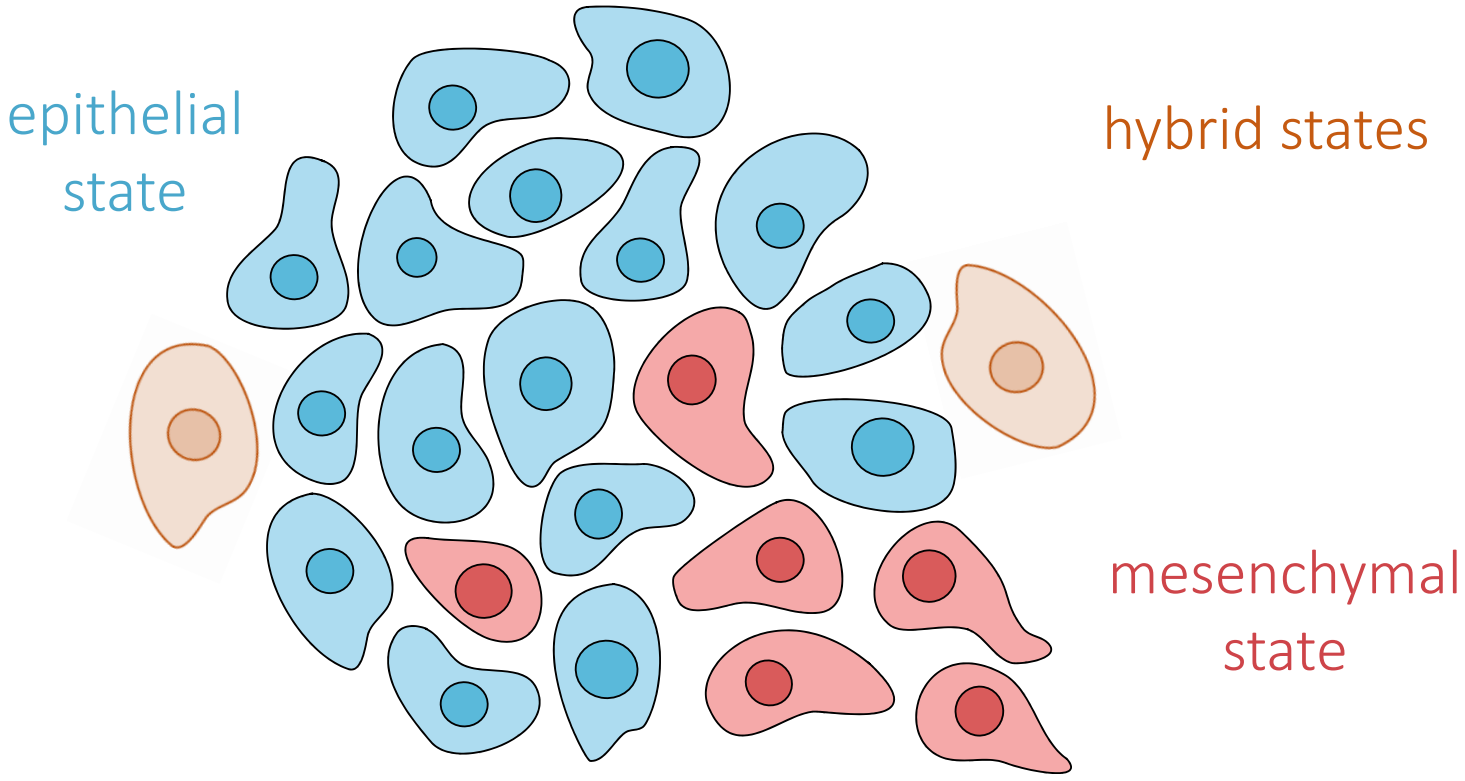
EMT and regulation of cell surface phenotype



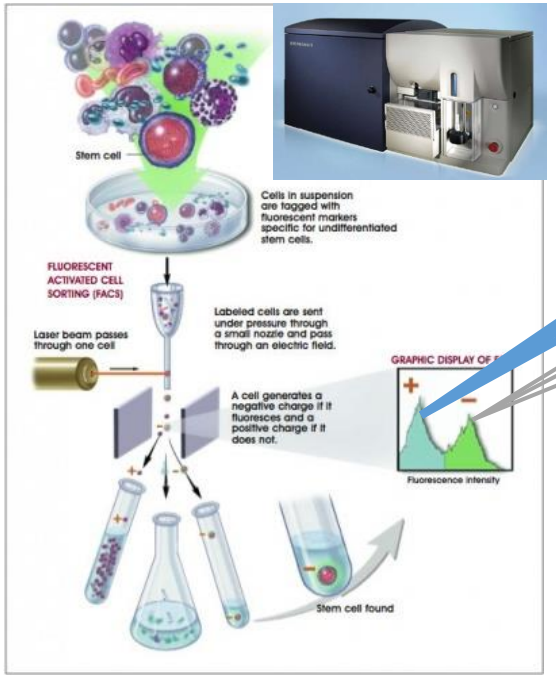
GENERAL HYPOTHESIS:
Cell surface mirrors cellular phenotype
Identification – Characterisation - Targeting

SOUČEK lab

Epithelial-mesenchymal plasticity contributes to intratumoral heterogeneity

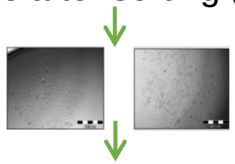


Flow cytometry as a tool for understanding of cell phenotype and function

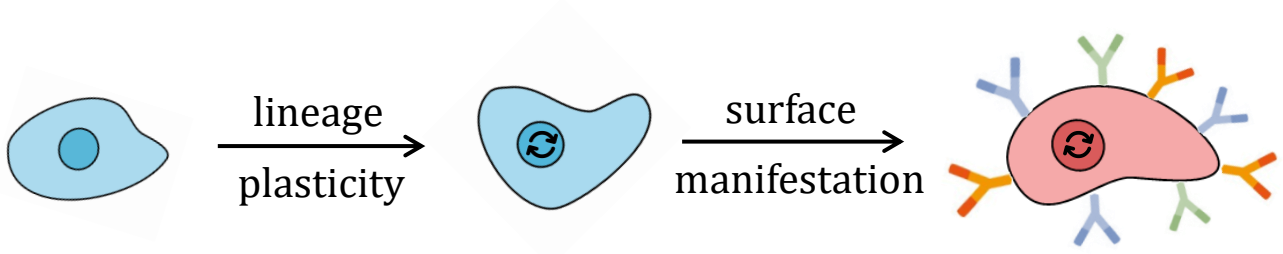


single cell/well
up to 384 well plate

re-culture after sorting (2D, 3D)



analysis: CyQuant, ATP, xCelligence, images, SEQ



Fedr, R., Pernicova, Z., Slabakova, E., Strakova, N., Bouchal, J., Grepl, M., Kozubik, A. & Soucek, K. Automatic cell cloning assay for determining the clonogenic capacity of cancer and cancer stem-like cells. ***Cytometry A 83, 472-482, (2013).***

Radek Fedr

Kahounova, Z., Kurfurstova, D., Bouchal, J., Kharaishvili, G., Navratil, J., Remsik, J., Simeckova, S., Student, V., Kozubik, A. & Soucek, K. The fibroblast surface markers FAP, anti-fibroblast, and FSP are expressed by cells of epithelial origin and may be altered during epithelial-to-mesenchymal transition. ***Cytometry A 93, 941-951, (2018).***

Zuzana Kahounová

Simeckova, S., Fedr, R., Remsik, J., Kahounova, Z., Slabakova, E. & Soucek, K. Multiparameter cytometric analysis of complex cellular response. ***Cytometry A 93, 239-248, (2018).***

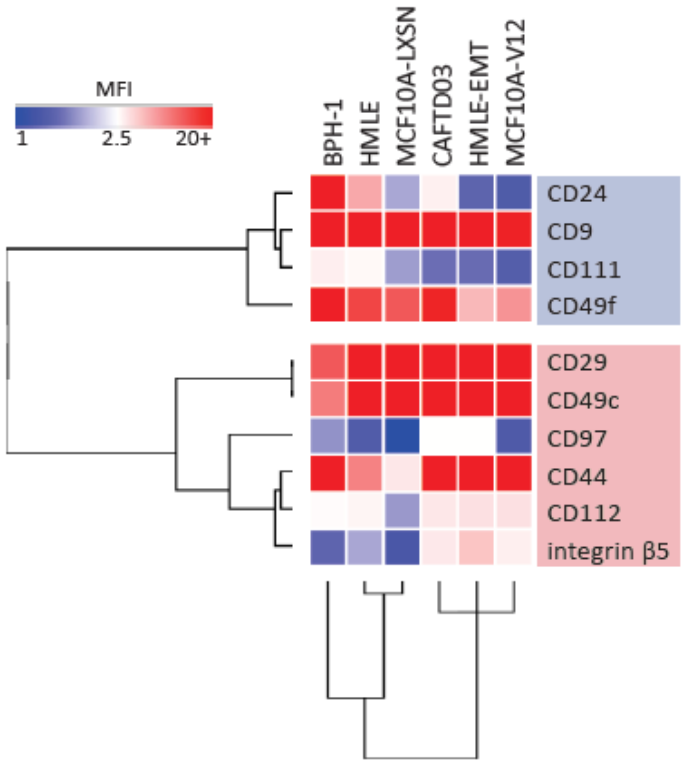
Šárka Šimečková

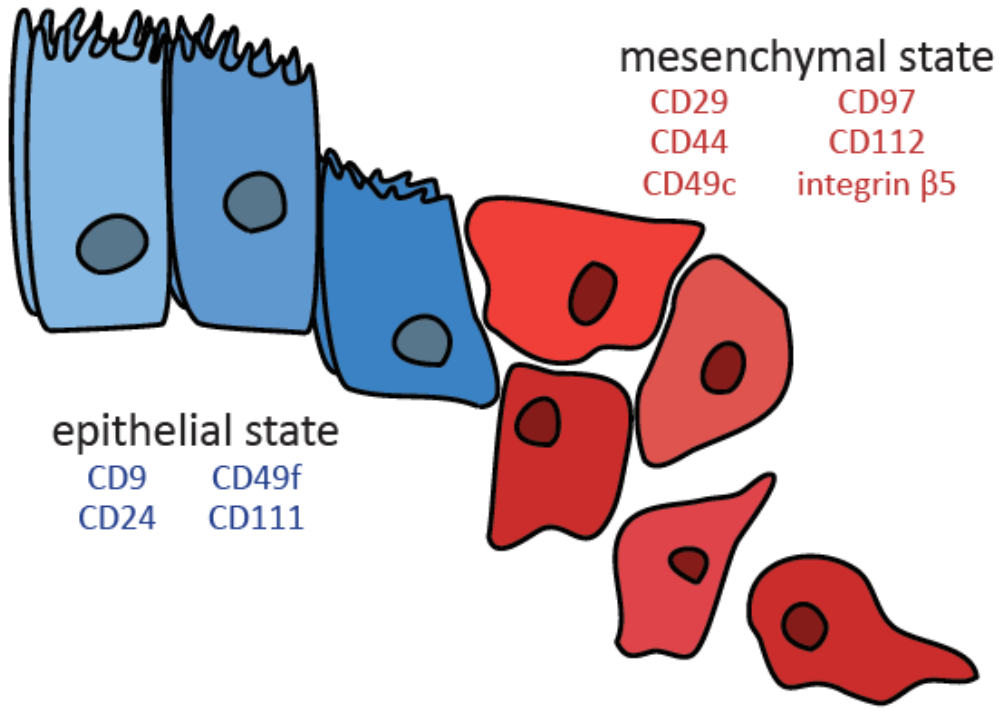
Drápela, S., Fedr, R., Remšík, J., Souček, K., High-throughput, parallel flow cytometry screening of hundreds of cell surface antigens using fluorescent barcoding. **Methods in Molecular Biology**, under review, (2021)

Stanislav Drápela

Cell phenotypes associate with distinct surface antigens *in vitro*

Hypothesis: The 10-molecule signature associates with plasticity of cancer cells





➔ 12-color cytometric panel for analysis of tumor heterogeneity

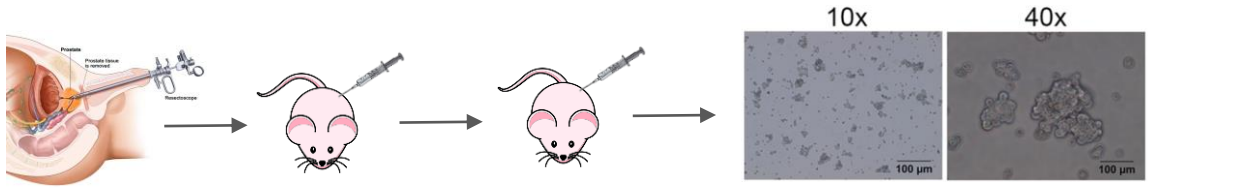
Remsik, J. et al. *Br. J. Cancer* ***118, 813-819, (2018).***

Six-molecular surface fingerprint predicts docetaxel resistance in prostate cancer patients

Stanislav Drápela

Taxane resistance = serious obstacle in the therapy of advanced prostate cancer

In vivo models – docetaxel-resistant patient derived xenografts



TURP → engrafted s.c. → **docetaxel** (33 mg kg^{-1})

van Weerden et al., *Br J Cancer*, ***2009***

STAGE	FIVE-YEAR SURVIVAL
LOCAL	>99%
REGIONAL	>99%
ADVANCED	29%

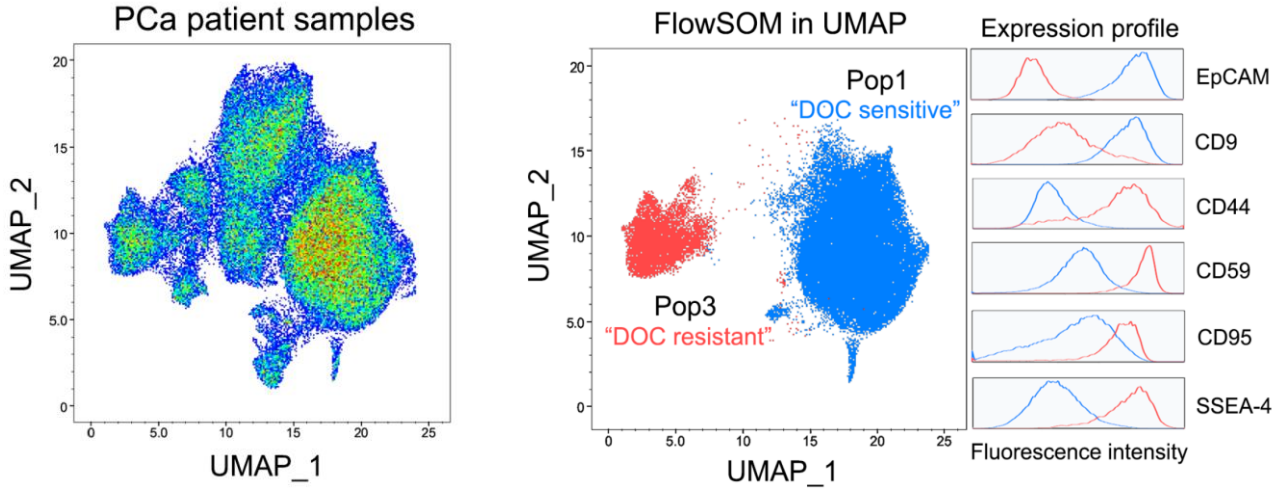
Data from Cancer Facts & Figures, *ACS*, ***2018***

Aim: To determine unique **surface fingerprint** of docetaxel-resistant (DR) cells

i. "personalized" prediction of docetaxel effectiveness prior therapy

ii. identification of druggable targets for the targeting of DR cells

iii. description of the mechanism of docetaxel resistance



Drápela, S., et al., *Pre-existing cell subpopulations in primary prostate cancer tumors display the surface fingerprint of docetaxel-resistant cells.* **Under revision.**

Docetaxel-resistant cell surface profile

↓EpCAM
epi cell adhesion molecule

↓CD9
tetraspanin

↑CD44
homing cell adhesion molecule

↑CD59
glycoprotein protectin

↑CD95
Fas receptor

↑SSEA-4
stage-specific embryonic antigen-4

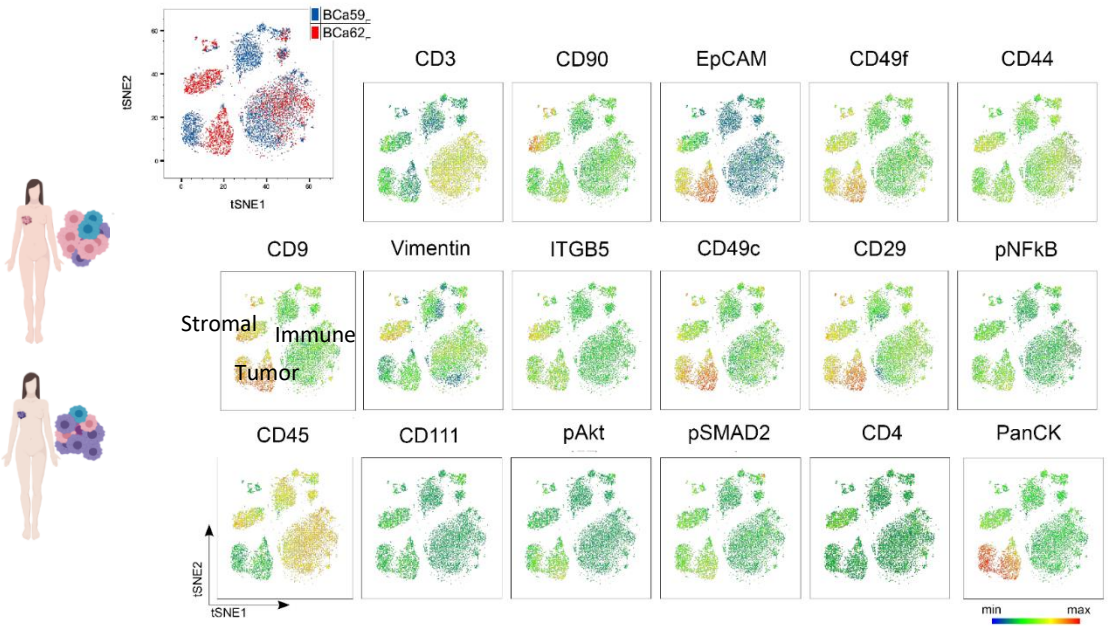
Plasticity and intratumoral heterogeneity in triple-negative breast cancer

Barbora Kvokačková

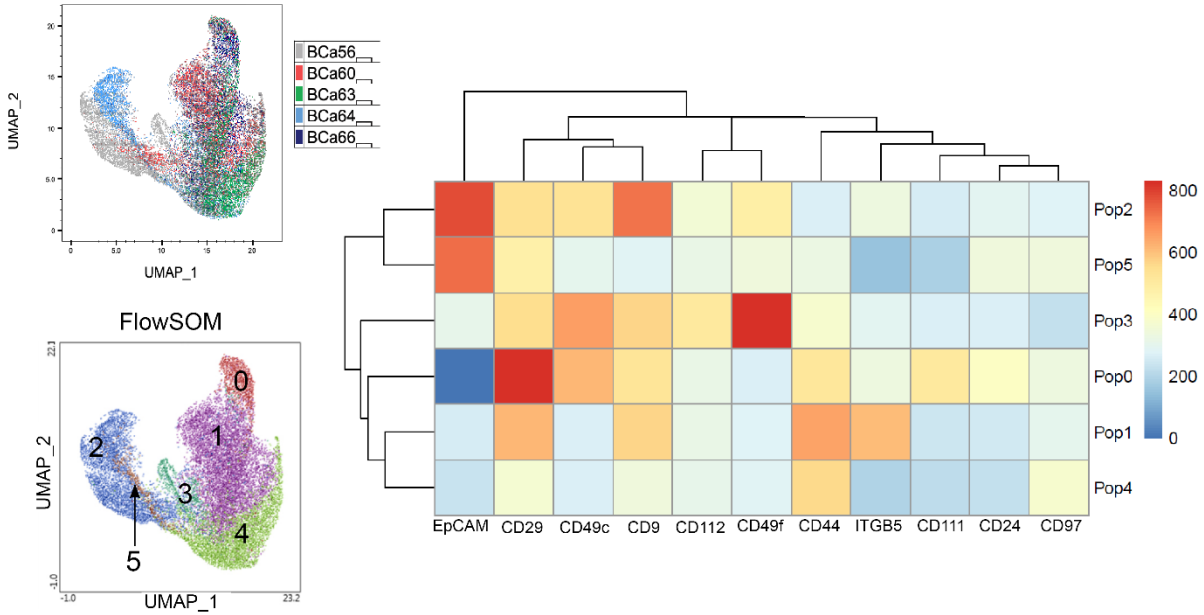
Brno Ph.D. Talent

- Complex analysis of tumor and microenvironmental compartments in TNBC samples by mass cytometry
- Analysis of epithelial-to-mesenchymal plasticity (EMT) in TNBC patient samples
- Identification of new clinically valuable biomarkers

➢ Complex heterogeneity in TNBC tissues (36 markers)



➢ EMT surface fingerprint in clinical specimens



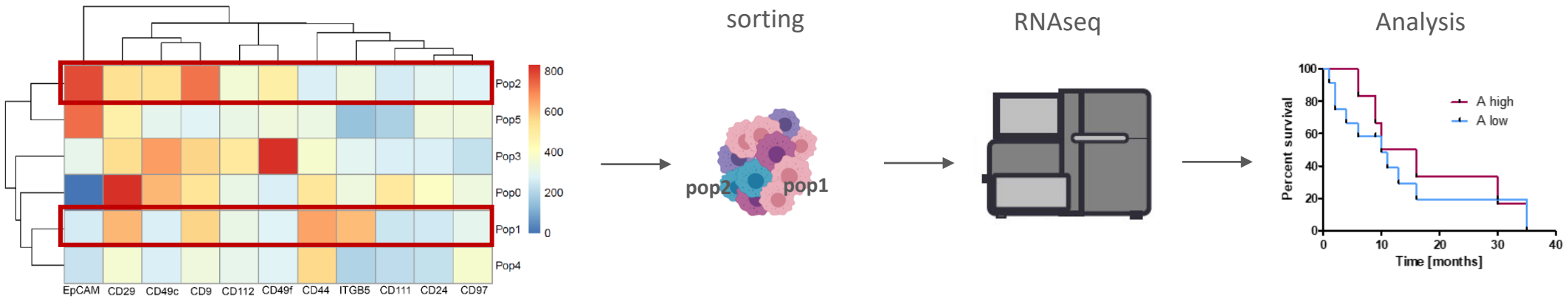
collaboration with MMCI MASARYK MEMORIAL CANCER INSTITUTE CLIP

Remsik, J. et al. Plasticity and intratumoural heterogeneity of cell surface antigen expression in breast cancer Br. J. Cancer 118, 813-819, (2018).

Future outlook

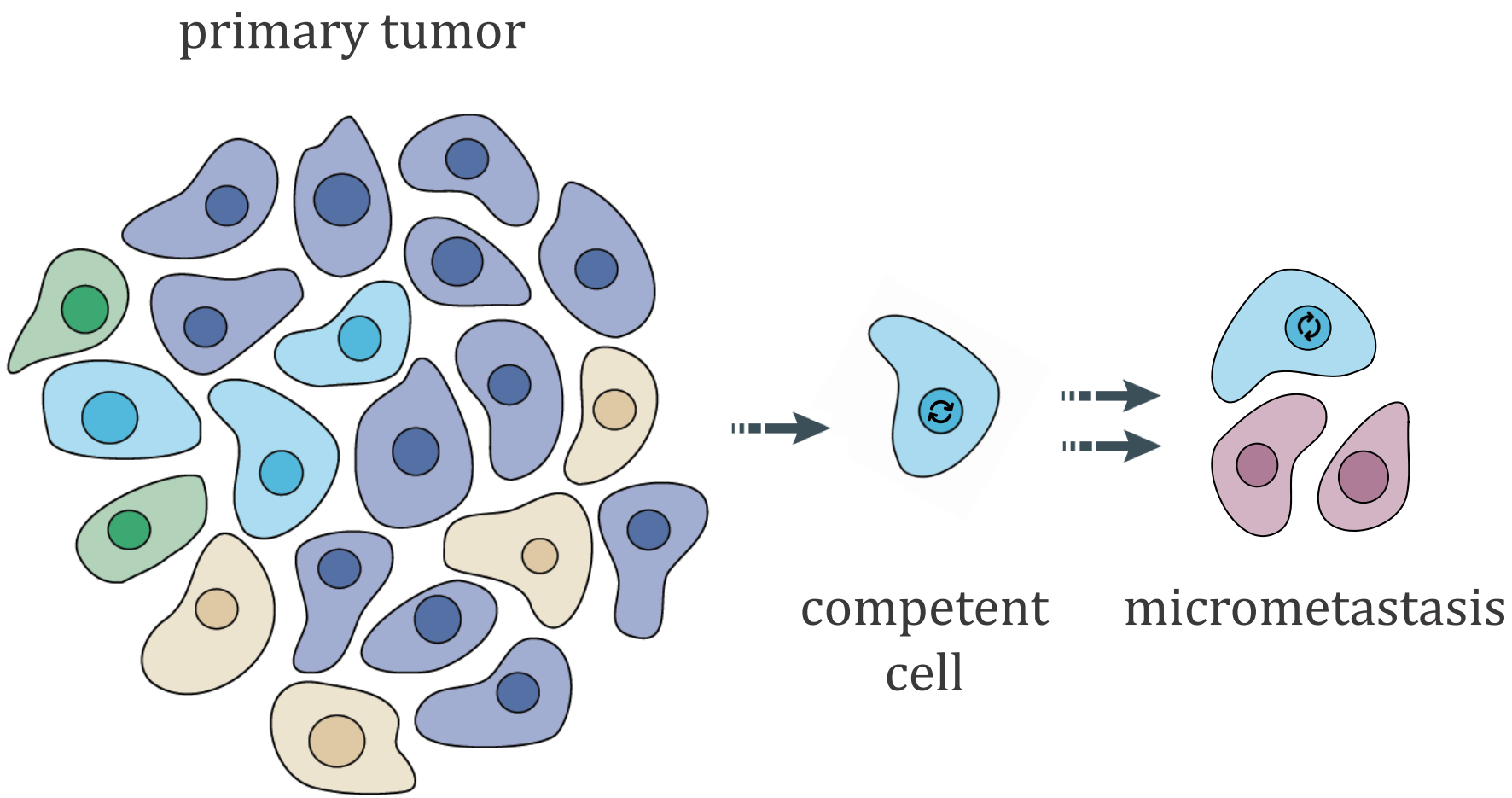
- Description of intratumoral and stromal heterogeneity in TNBC patient cohort by mass cytometry – advanced data analysis

- Identification of genetic signatures in selected subpopulations and their association with clinical observations



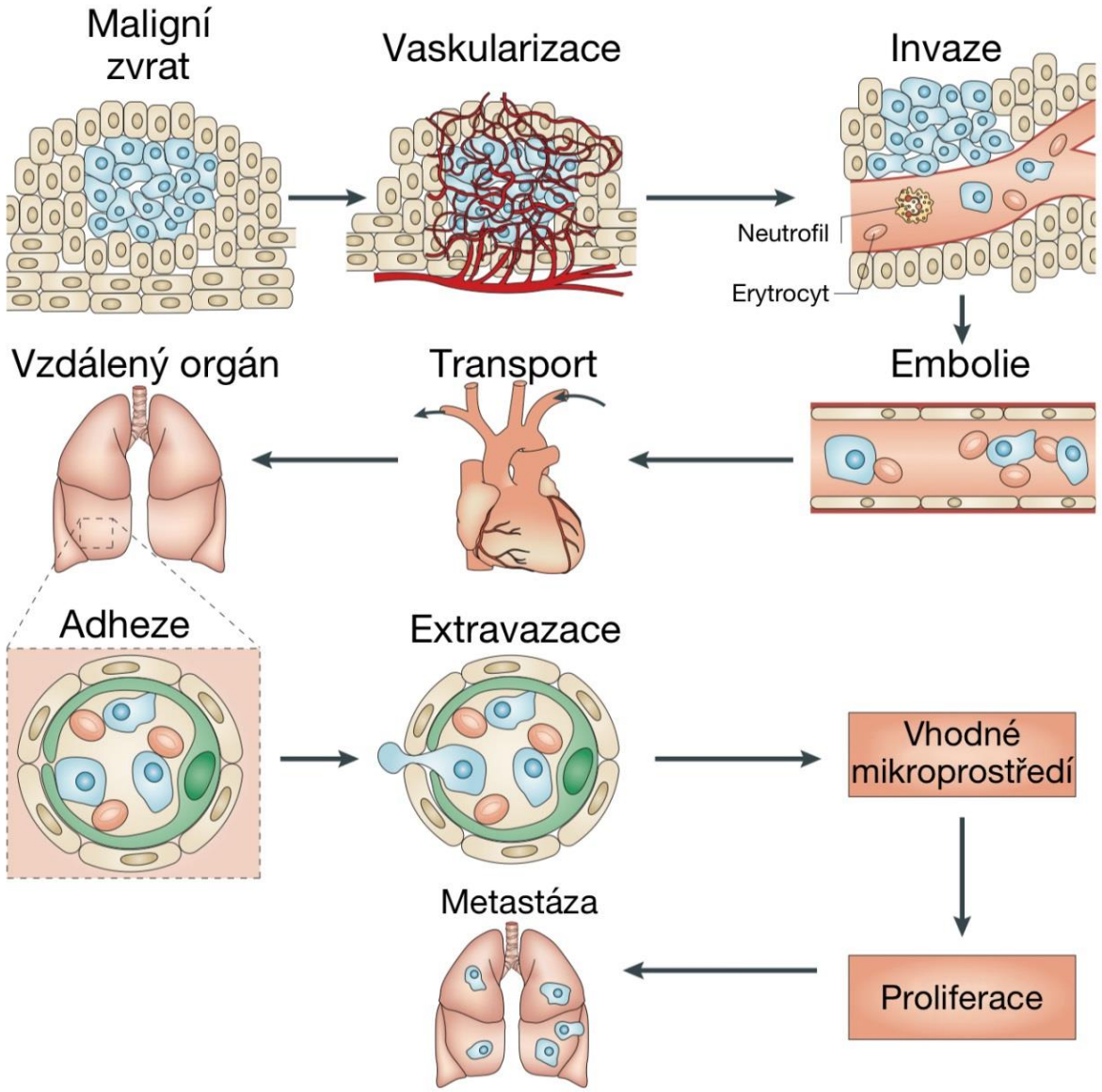
- Validation of identified biomarkers by IHC on retrospective cohort of TNBC patients

What kind of cells and mechanisms drive metastasis and chemoresistance?



Metastatická kaskáda

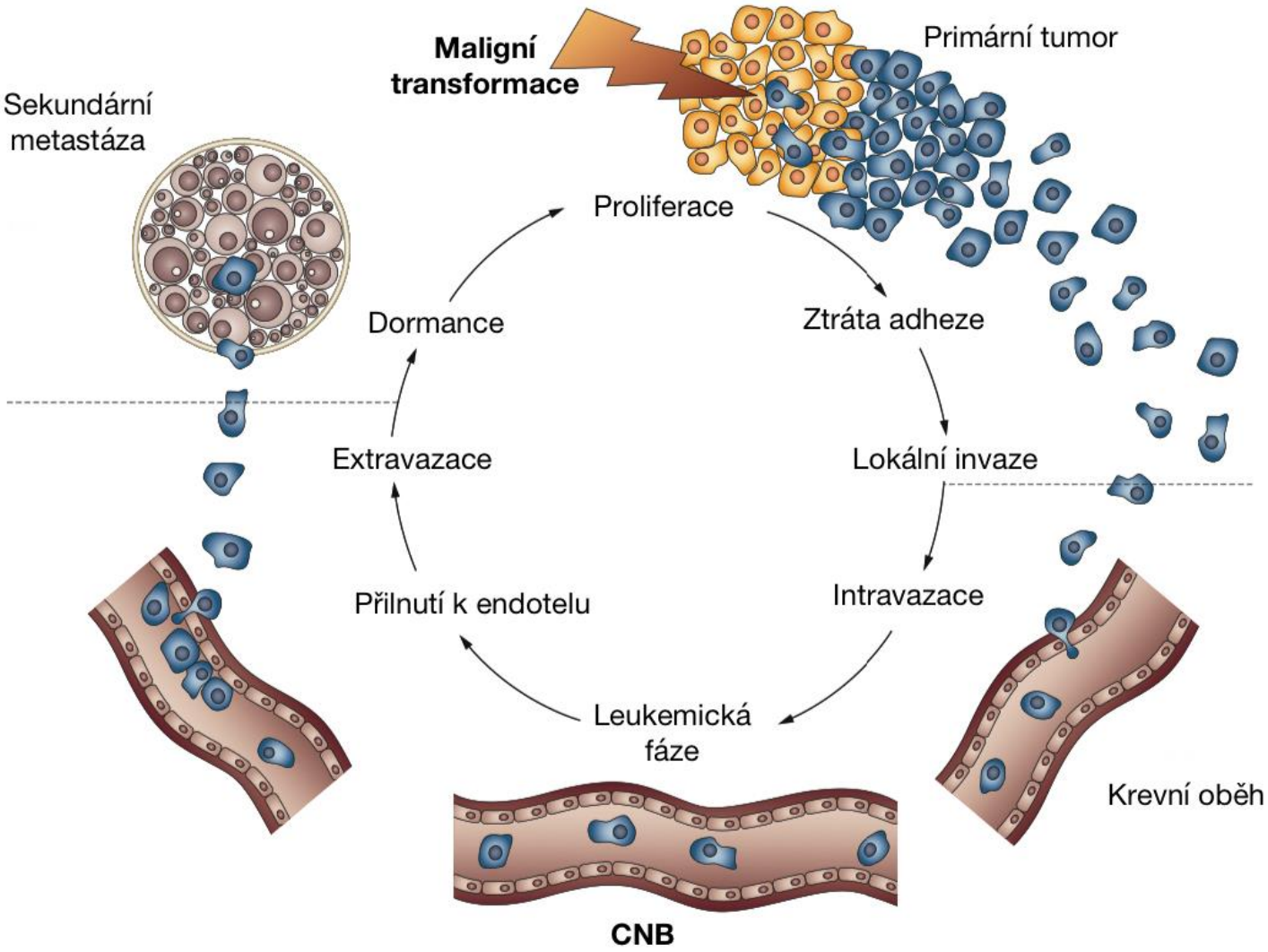
Cirkulující nádorové buňky (CNB) – klíčová úloha



Francia et al., *Nat. Rev. Cancer* (2011)

Proč se cirkulujícími nádorovými buňkami zabývat?

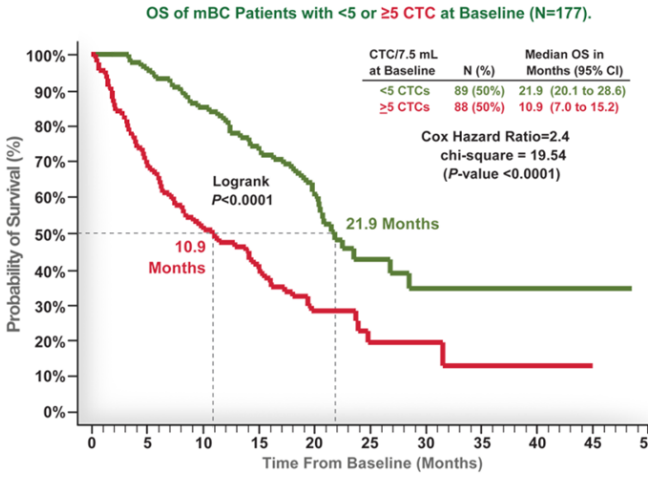
- 90% úmrtí spojených se solidními nádory – **metastáze**
  - Šíření primárně krví
- Klinicky významné
  - „Liquid biopsy“
  - Průběh terapie
  - Prognostický znak
  - Specifické mutace → cíle terapie



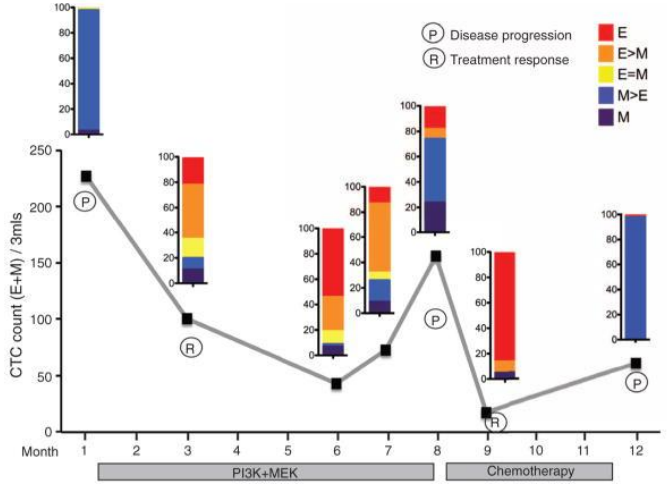
Schilling, *et al.*, *Nat. Rev. Urol.* (2012)

Clinical relevance of circulating tumor cells

1. Quantification of CTCs

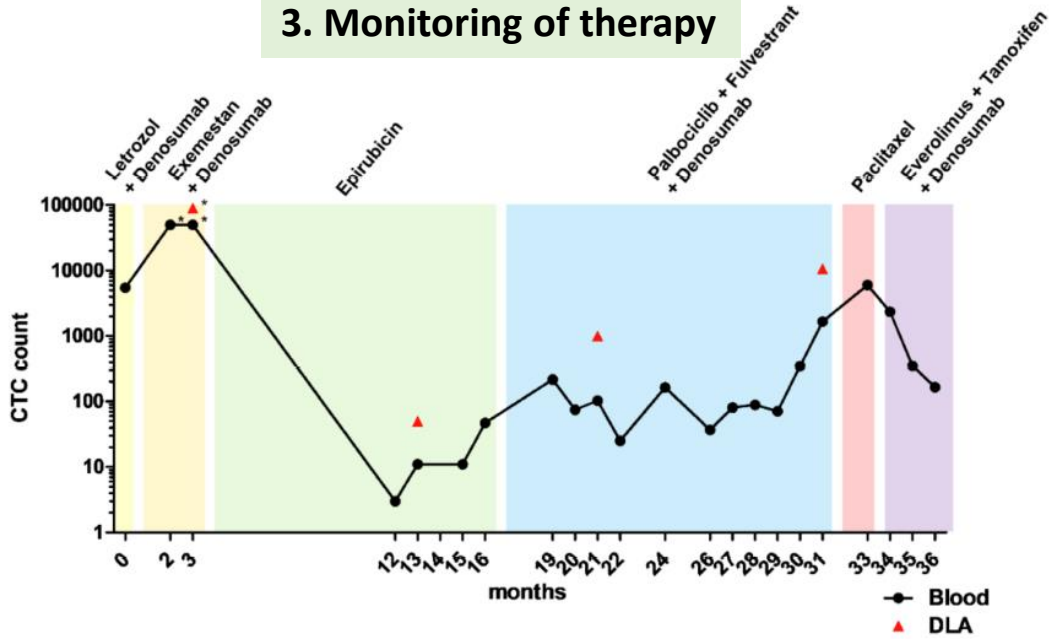


2. E/M phenotypization of CTCs



Yu *et. al.,* Science, 2013

3. Monitoring of therapy



Frankers *et. al.,* Cancers, 2021

1) **QUANTIFICATION:** high numbers correlates with increased risk of metastasis

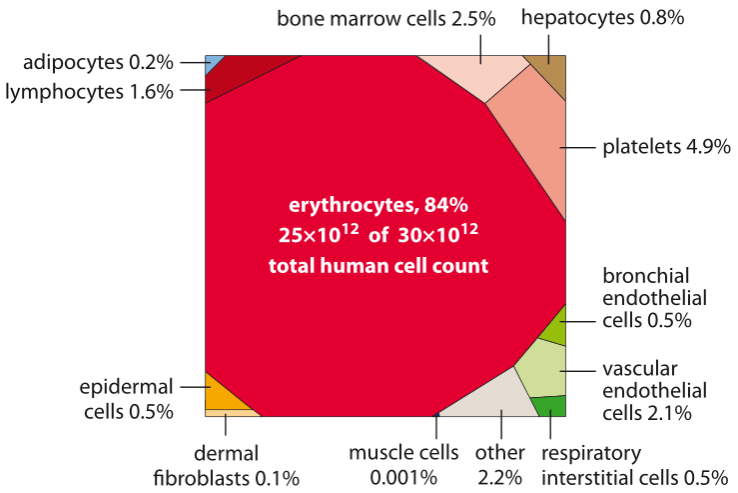
2) **PHENOTYPIZATION:** E/M phenotype of CTCs predicts chemoresistance

3) **MONITORING** of chemotherapy efficiency for better therapeutical strategies

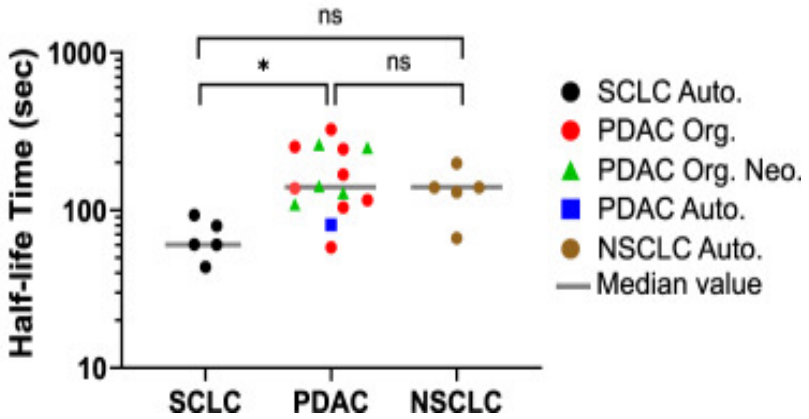
SOUČEK lab

Technical challenges for detection of circulating tumor cells

1. Frequency of CTCs

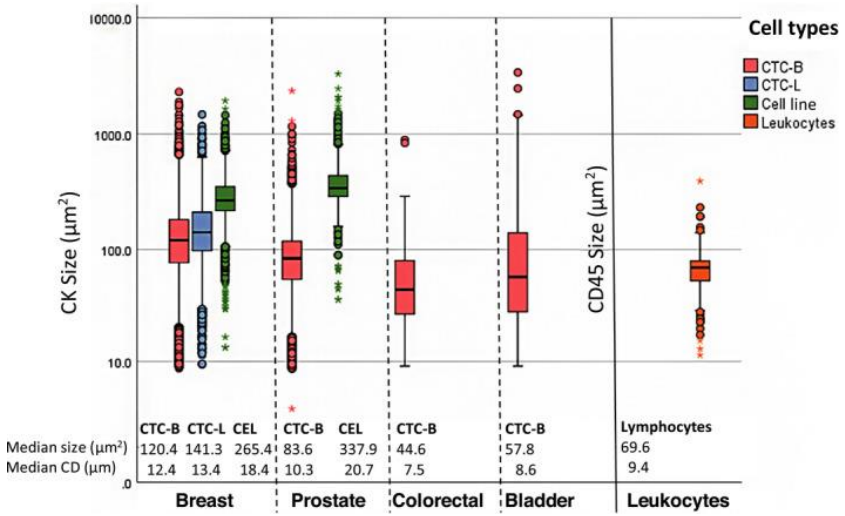


2. Half-life time of CTCs



Hamza *et al.*, Nat Commun, 2021

3. Size of CTCs



Mendelaar *et al.*, Mol Oncol, 2021

1) **FREQUENCY:** CTCs frequency is about 1-10 /10 ml of human blood

2) **HALF-LIFE TIME**: Half-life time of CTCs in range of minutes

3) **SIZE:** Comparable size with leukocytes

Flow cytometry as one option for CTCs detection

<u>Lack of common/specific CTCs markers</u>

SOUČEK lab

Klinické využití detekce cirkulujících nádorových buněk

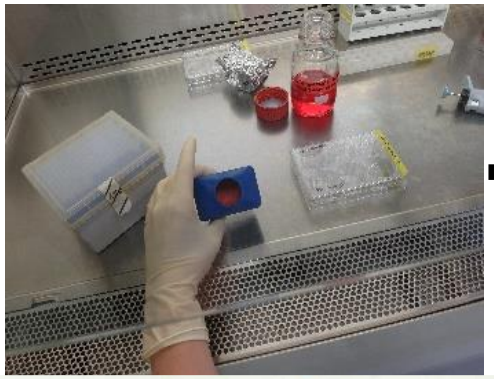
- Odhad prognózy pacienta
- **Monitoring průběhu onemocnění**
- Včasná detekce

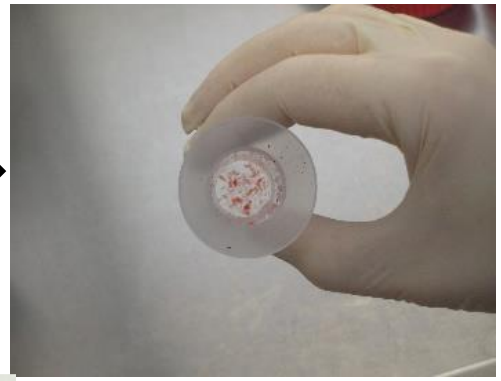
- Metastázující karcinomy prsu a prostaty – hranice 5 CNB/7,5ml
- Metastázující karcinom tlustého střeva – hranice 3 CNB/7,5 ml
- CellSearch system Veridex – schváleno FDA

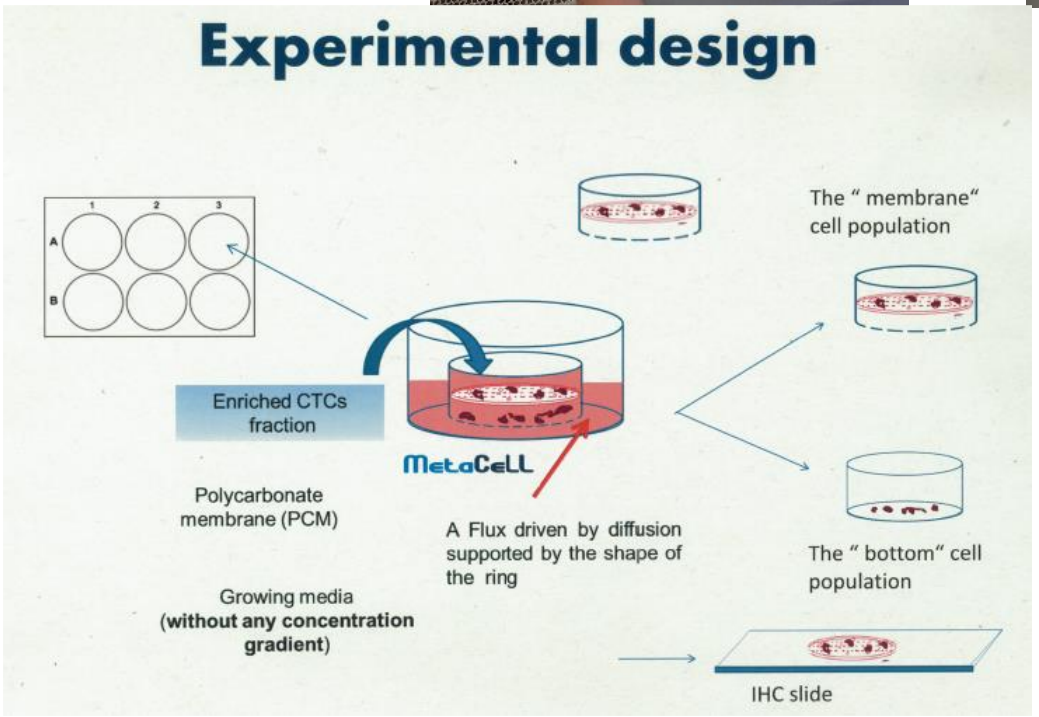
www.cellsearchctc.com

Příklad: Filtrace

- polycarbonate membrane with 8 μm pores (CTCs over 20 μm)
- capilary force-driven filtration

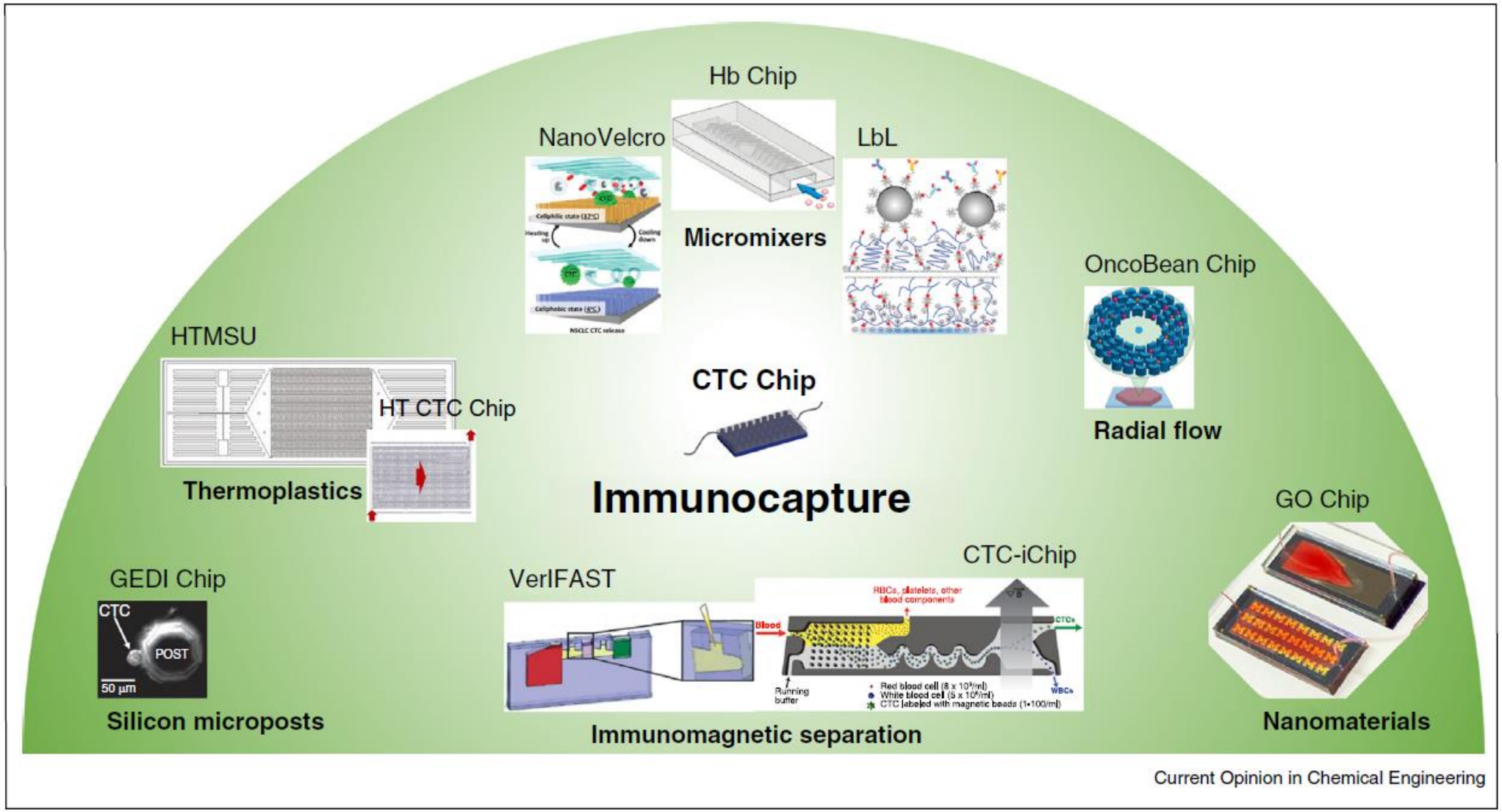




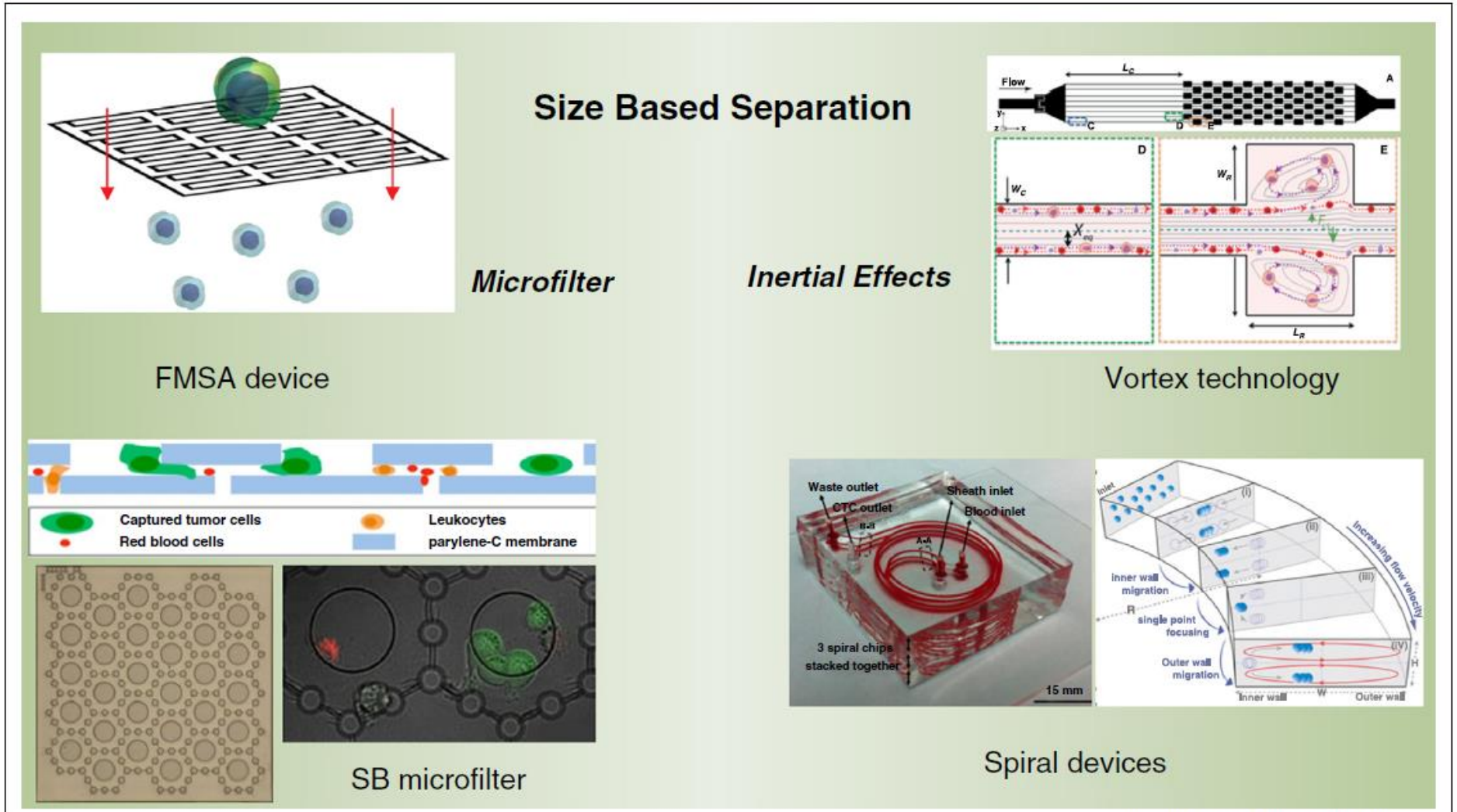


MetaCell

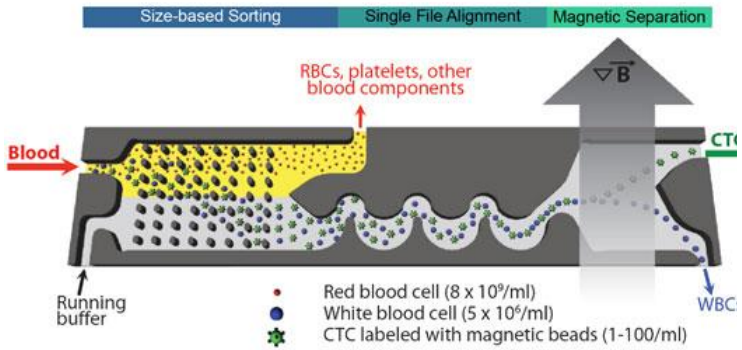
Příklad: mikrofluidní separace

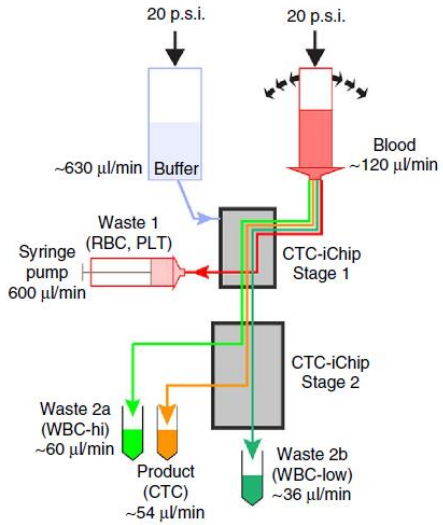


Příklad: mikrofluidní separace



Příklad: mikrofluidní separace





CTC-iChip running platform

PROTOCOL

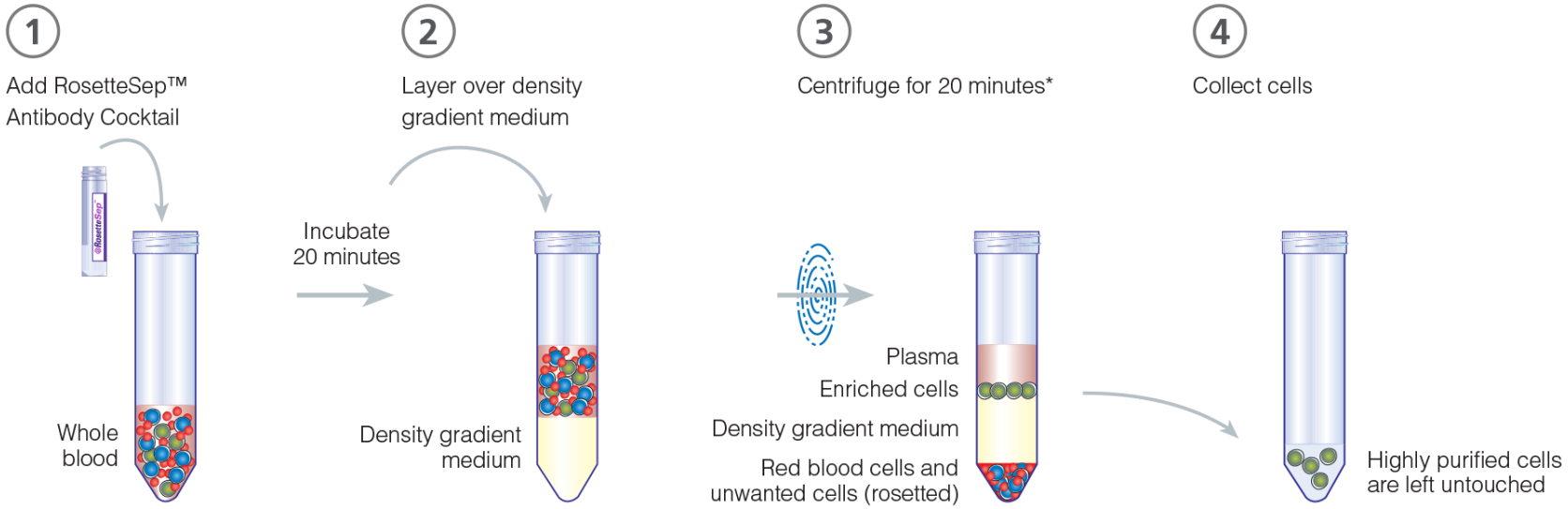
Microfluidic, marker-free isolation of circulating tumor cells from blood samples

Nezihi Murat Karabacak[1,4], Philipp S Spuhler[1,4], Fabio Fachin[1], Eugene J Lim[1], Vincent Pai[1], Emre Ozkumur[1], Joseph M Martel[1], Nikola Kojic[1], Kyle Smith[1], Pin-i Chen[1], Jennifer Yang[1], Henry Hwang[1], Bailey Morgan[1], Julie Trautwein[2], Thomas A Barber[1], Shannon L Stott[1,2], Shyamala Maheswaran[2], Ravi Kapur[1], Daniel A Haber[2,3] & Mehmet Toner[1]

[1]Department of Surgery and Center for Engineering in Medicine, Massachusetts General Hospital, Boston, Massachusetts, USA. [2]Cancer Center, Massachusetts General Hospital, Boston, Massachusetts, USA. [3]Howard Hughes Medical Institute, Chevy Chase, Maryland, USA. [4]These authors contributed equally to this work. Correspondence should be addressed to M.T. (mtoner@hms.harvard.edu).

Published online 27 February 2014; doi:10.1038/nprot.2014.044

Izolace CTC pomocí deplece CD45+ buněk krve

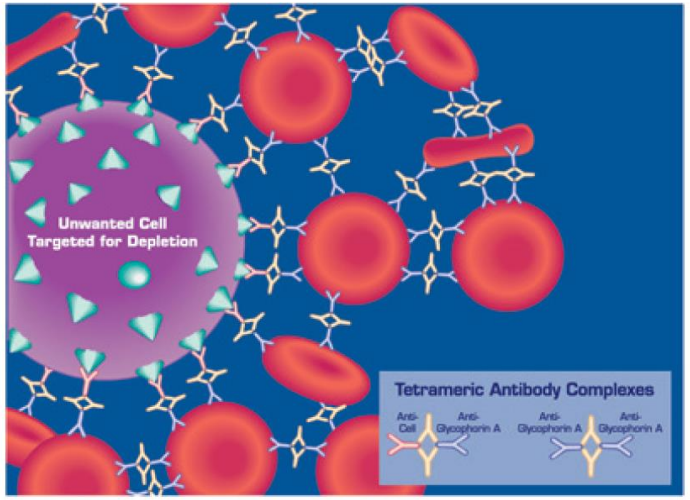


*Use SepMate™ to reduce centrifugation time to 10 minutes with brake on.

RosetteSep™

Unique Immunodensity Cell Isolation

RosetteSep™ kits offer one-step enrichment of cells directly from human whole blood. By crosslinking unwanted cells to red blood cells (RBCs) present in the sample, CTCs are enriched during standard density gradient centrifugation. RosetteSep™ is easy to use, does not require additional equipment, reduces sample handling time and maximizes convenience. RosetteSep™ can be easily combined with **SepMate™**, a specialized isolation tube that standardizes and minimizes variability when isolating cells using density gradient centrifugation. Learn more at **www.RosetteSep.com** and **www.SepMate.com**.



RosetteSep™

CD45 Depletion Cocktail for Enrichment of Circulating Epithelial Tumor Cells

For labeling 200 mL blood

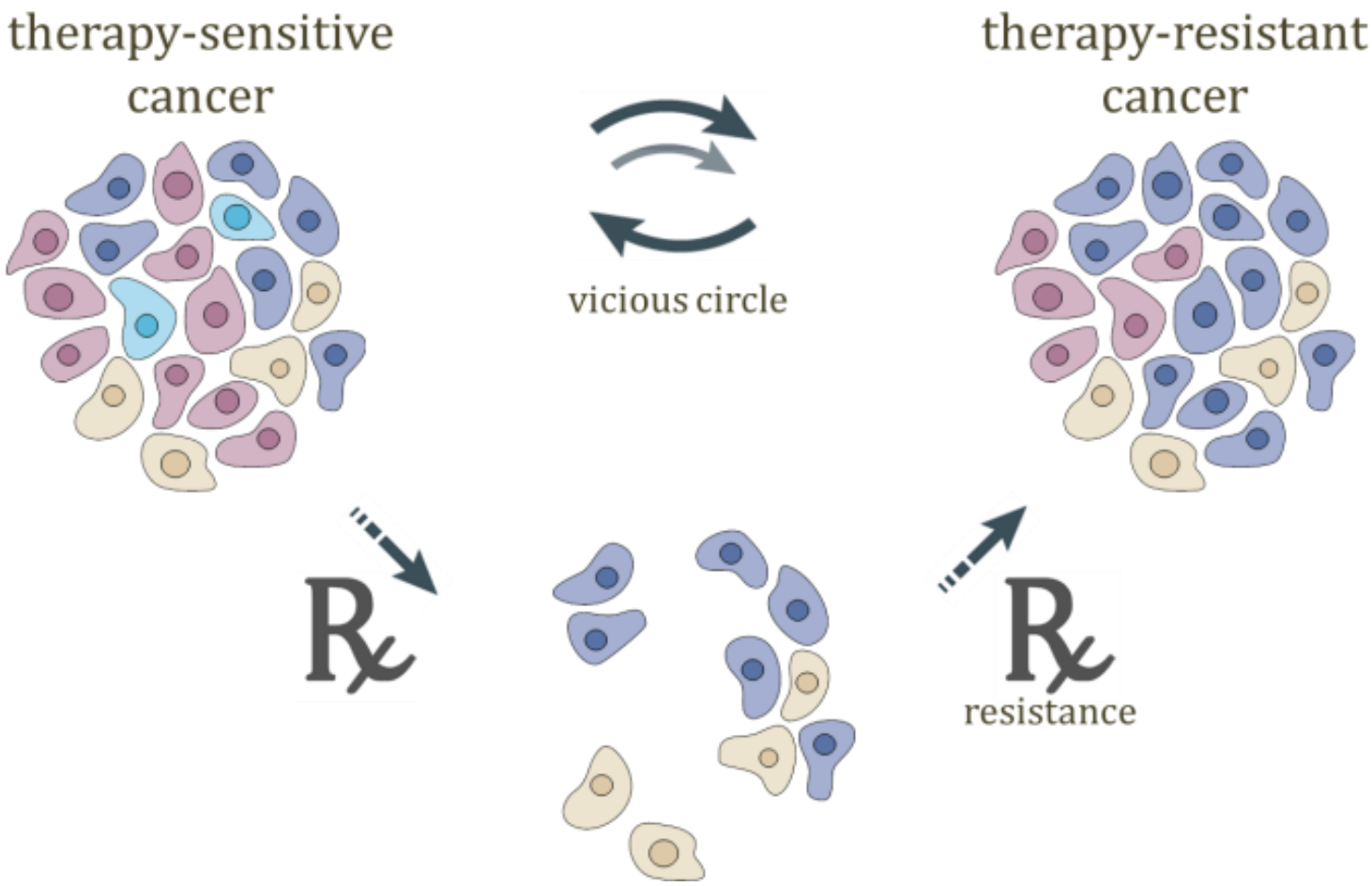
Kit Contains:
CD45 Depletion Cocktail for Enrichment of Circulating Epithelial Tumor Cells (5 x 2 mL)

Catalog #15162
Lot #00000

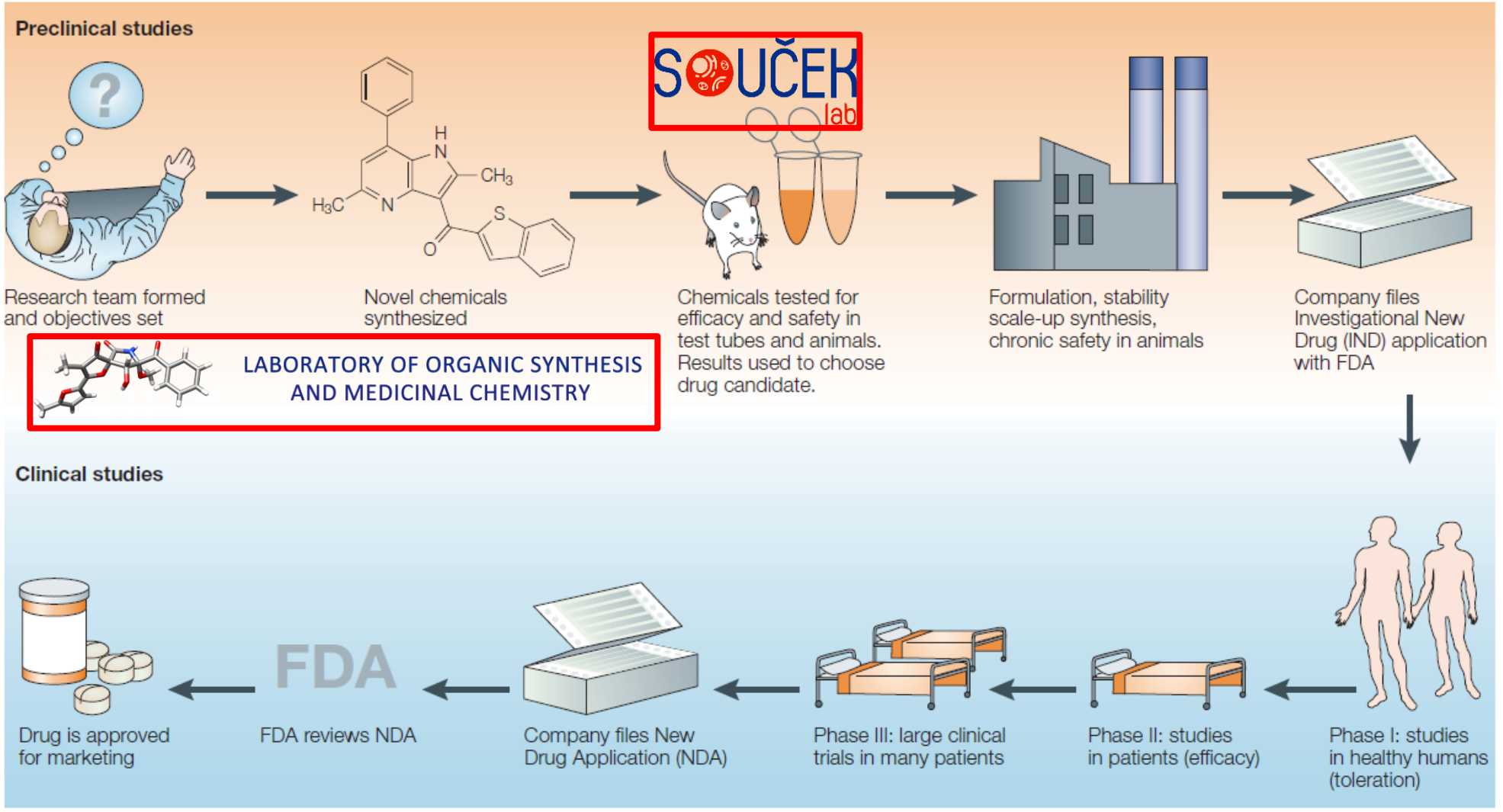
Store at 2-8˚C

FOR RESEARCH USE ONLY

Is there a cure for advanced cancer?



Cesta k novému léčivu – z laboratoře k pacientovi



IBP Institute of Biophysics

FNUSA ICRC

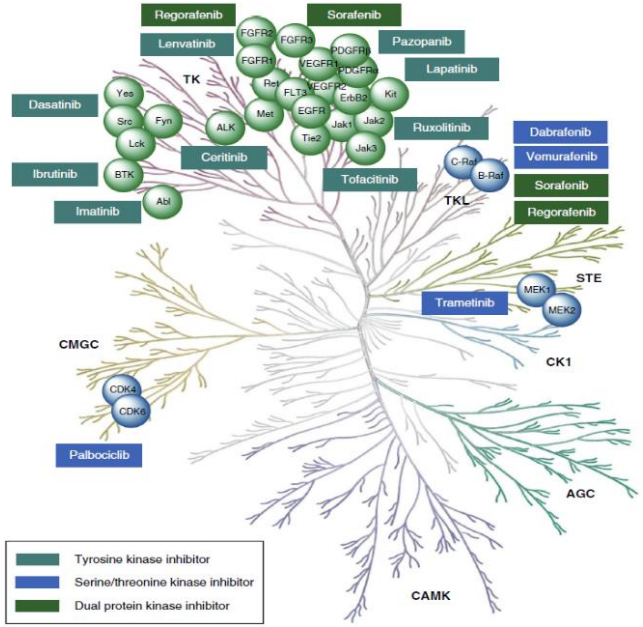
MUNI

zdroje – Lombardino et al. Nat.Rev. 2004

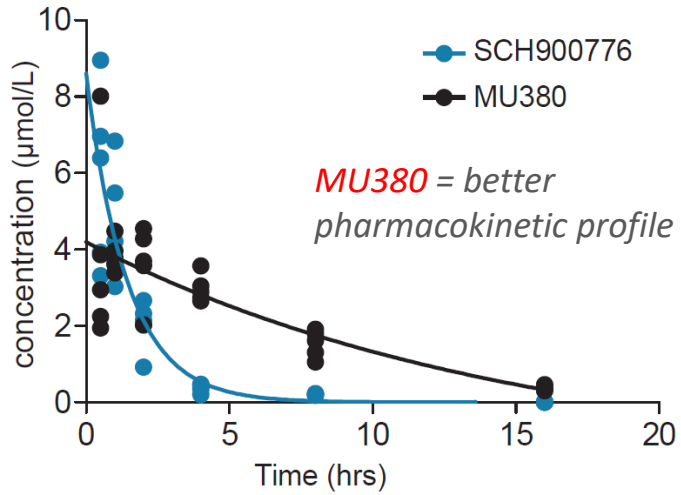
Protein kinases: promising targets for anticancer therapy

- ***> 500 enzymes*** *(approx. 1.7% of human genome)*
- *Kinases = phosphotransferases*
  - *regulation of multiple cell processes*
  - *DNA damage response, DNA repair, mitosis*

- *Protein kinase **inhibitors** = hot topic in pharmacology*
  (> 30 compounds in clinical trials)



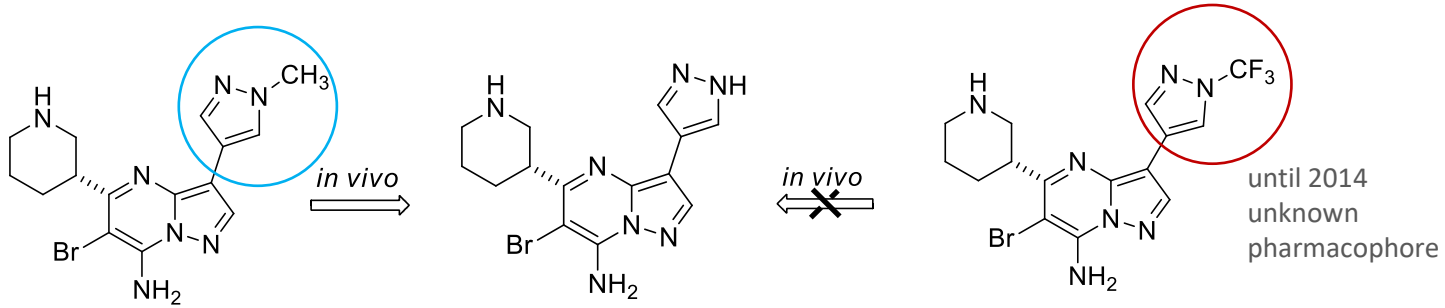
Pharmacokinetics



MU380 = better pharmacokinetic profile

Checkpoint kinase 1 (CHK1)

- *implemented in DNA damage response and DNA repair*
- *promising therapeutic target*
  - *novel CHK1i – **MU380***
- *synthetic lethality (gemcitabine, cytarabine)*



SCH900776
CHK1 IC_{50} = 0.005 mM
phase II clinical trials (with cytarabine)

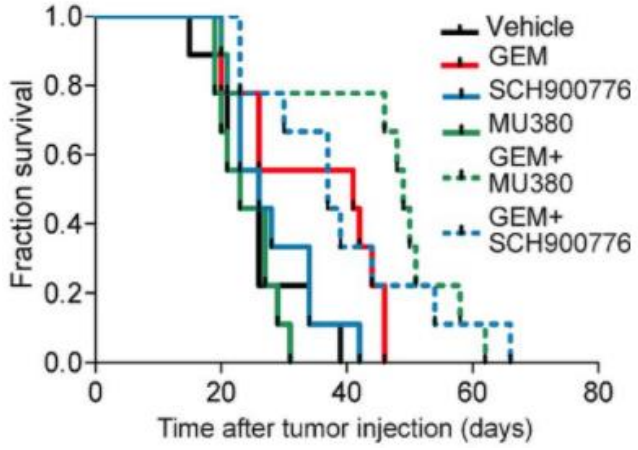
MU379
potential metabolite
less selective than SCH900776

MU380
CHK1 IC_{50} = 0.002 mM
more potent than SCH900776 in vitro

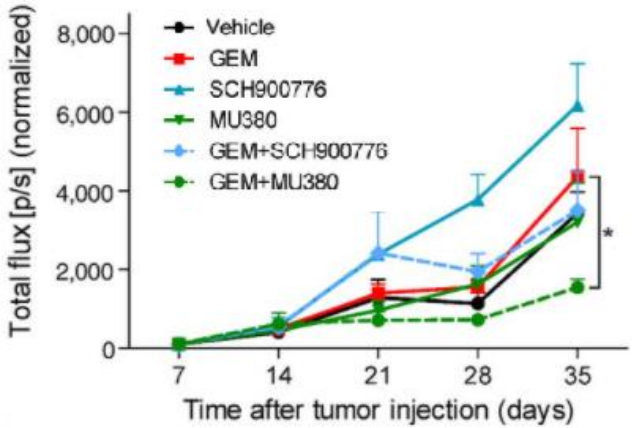
Kamil Paruch

CHK1 inhibition in multiple preclinical models

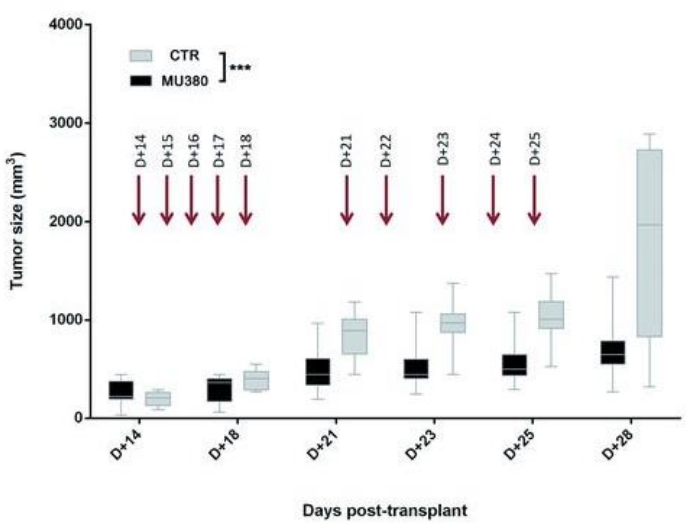
Ovarian cancer - survival

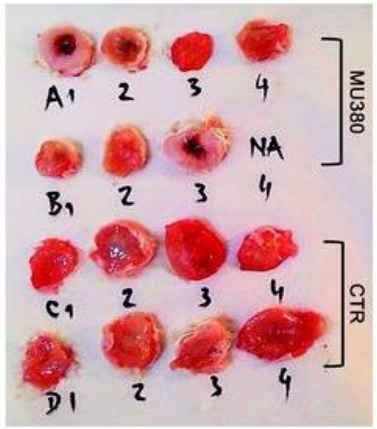


Pancreatic cancer

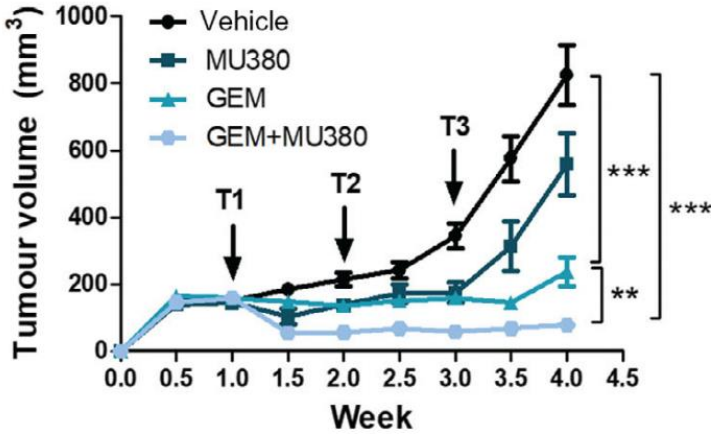


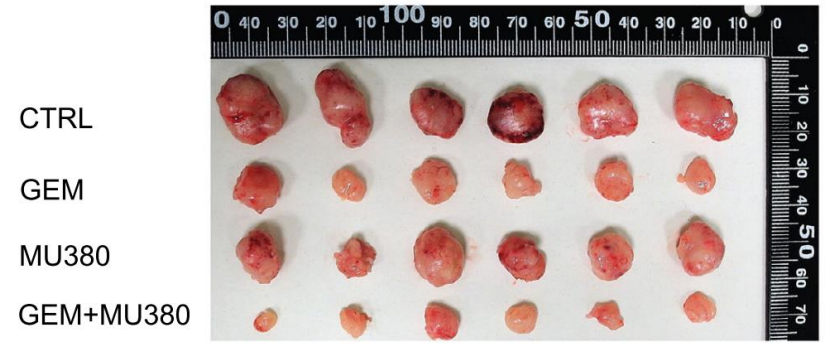
Chronic lymphocytic leukaemia (CLL)





Docetaxel-resistant prostate cancer (PCa)



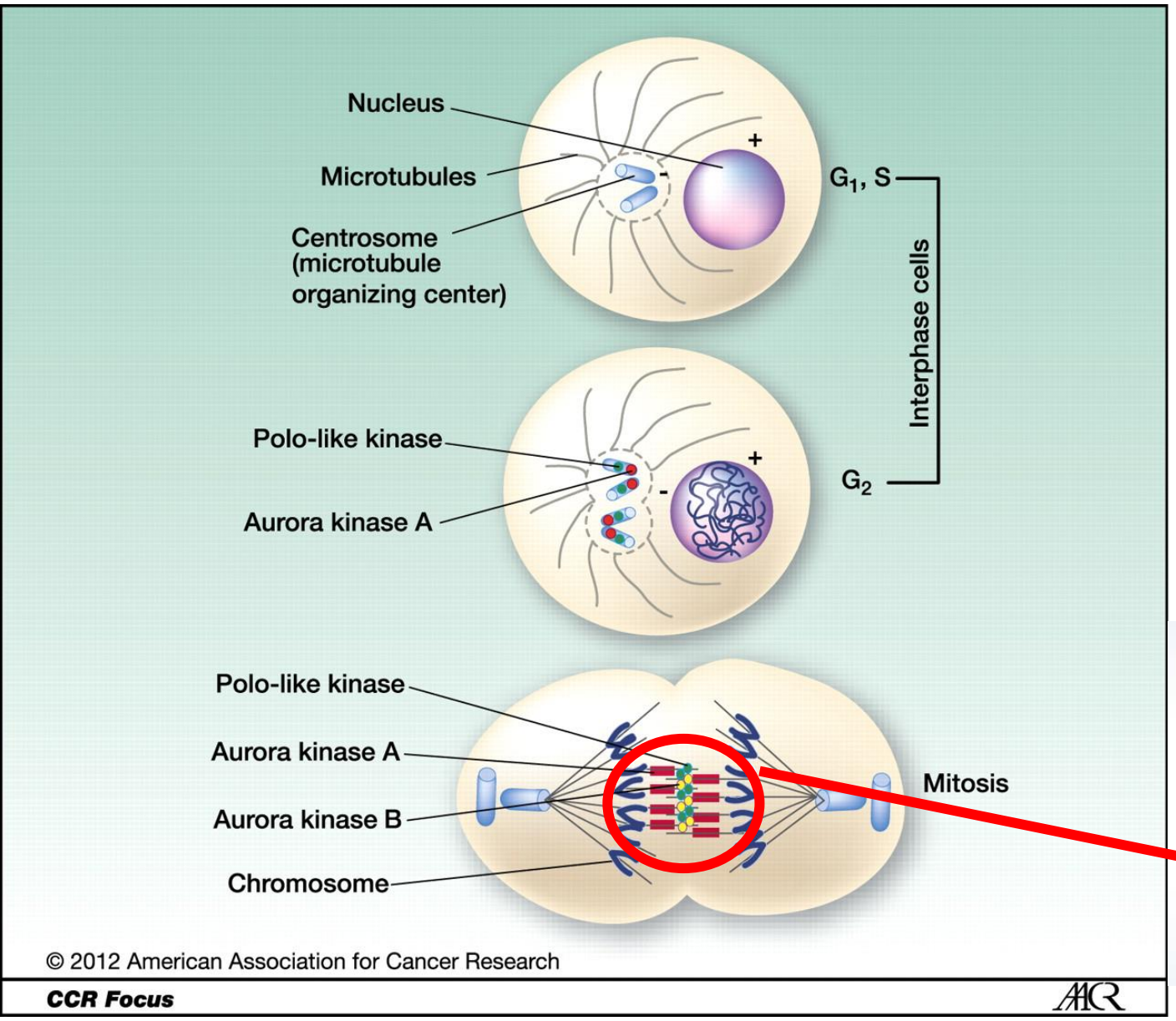


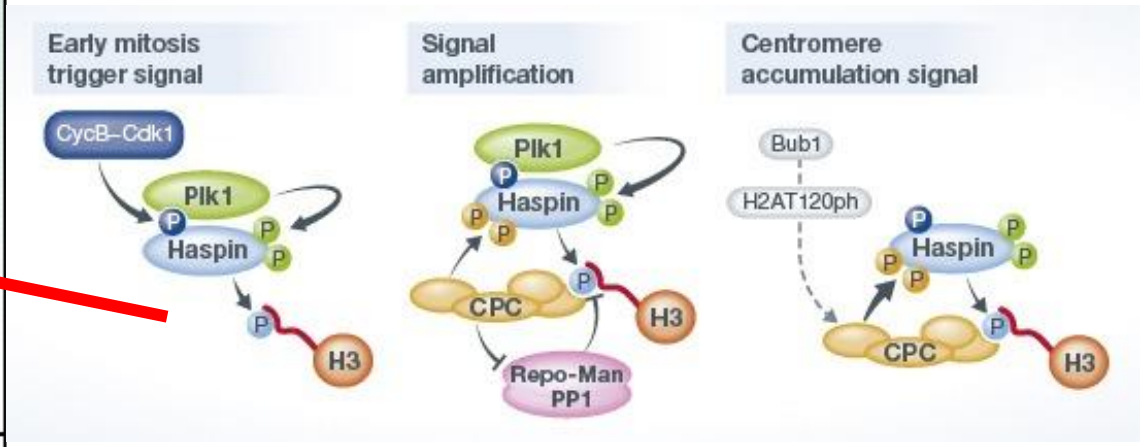
- *in vivo robust pharmacophore*
- *highly efficicent in combination with **antimetabolites** on various preclinical models*
- *bypasses chemoresistance in prostate cancer*
- *effective as monotherapy in CLL*

Kamil Paruch, Lumír Krejčí, Martin Trbušek

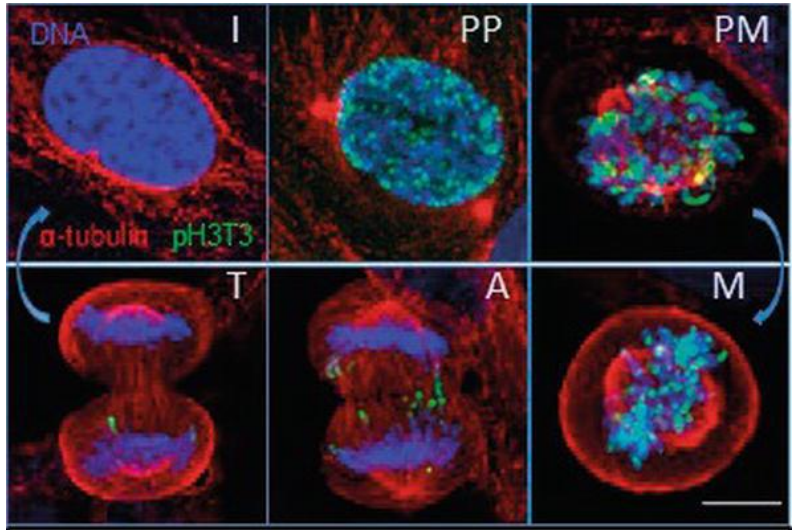
Cílení mitotického aparátu

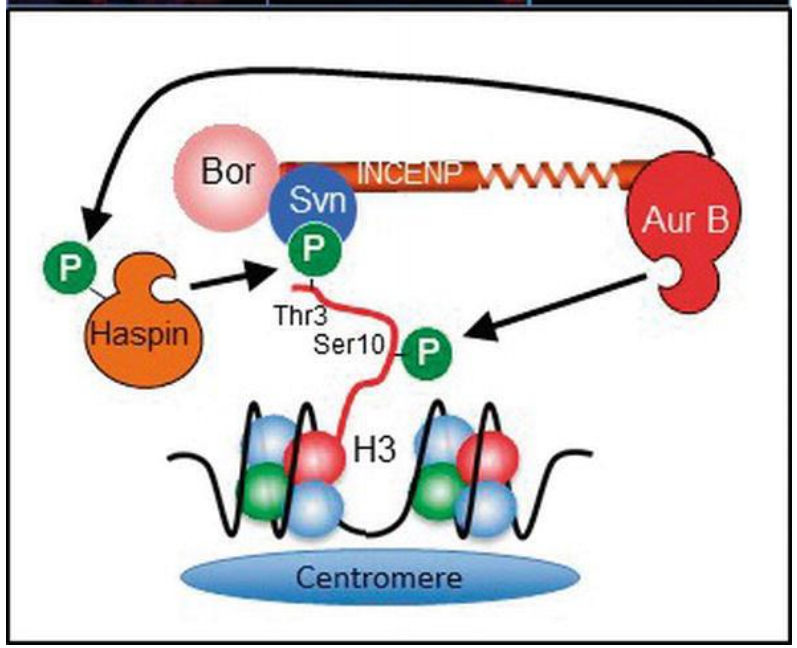
- Velké množství kináz, které jsou zásadní pro správné rozdělení genetického materiálu do dceřiných buněk
- Stále však není dostatek selektivních inhibitorů
- Kináza Haspin – společně s kinázou Aurora B součást CPC (chromosomal passenger complex) zásadního pro rozdělení chromatid

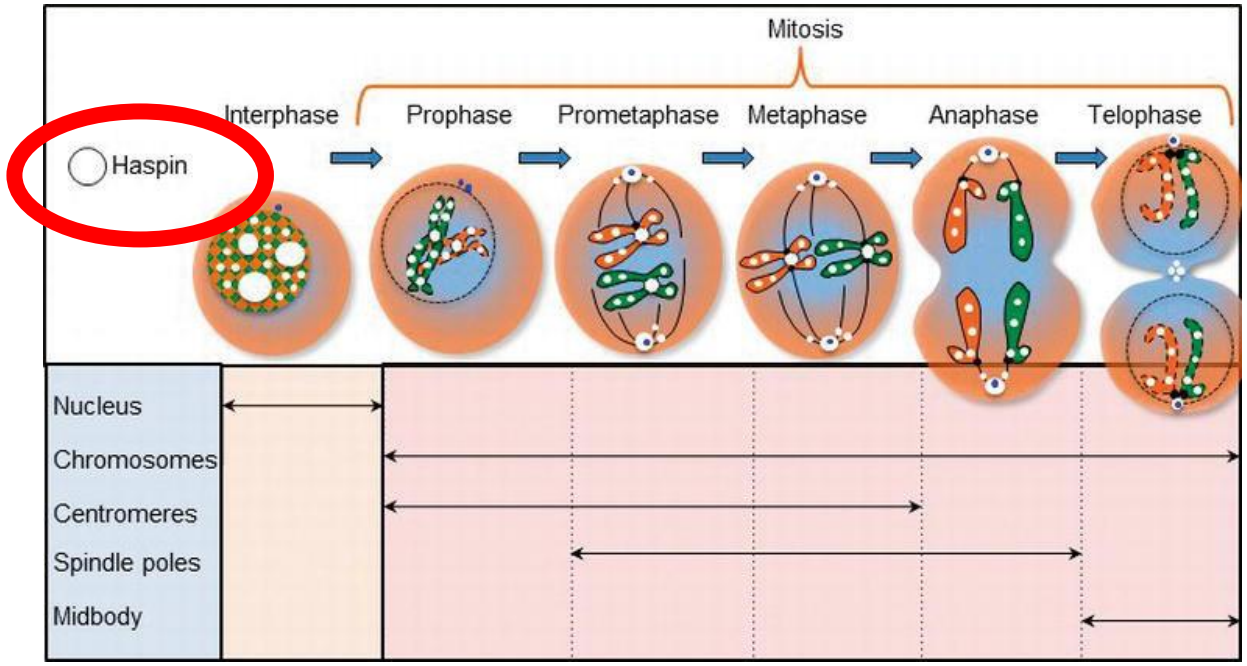


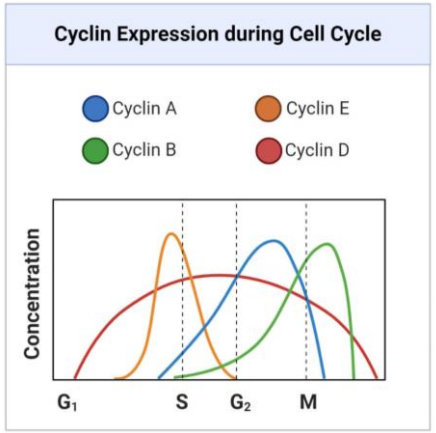


Kináza Haspin a proč ji studovat









X

Kontinuální exprese kinázy Haspin je zcela neobvyklá v porovnání s ostatními regulátory cyklu – potenciál pro úspěšné (selektivní) cílení léčivy

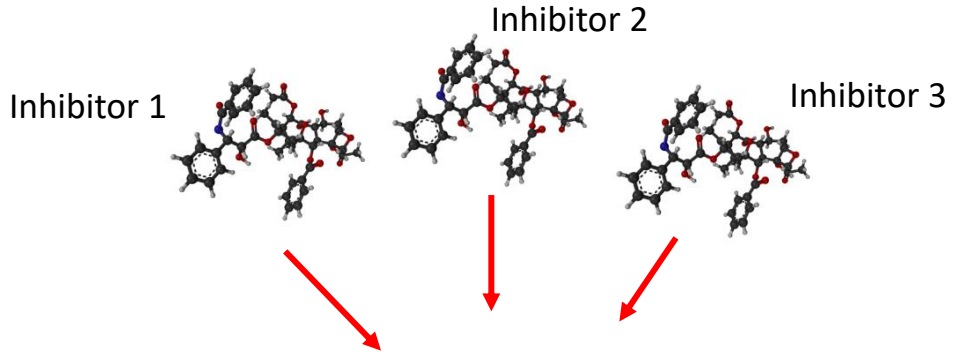
zdroje – Feizbakhsh et al. IntechOpen, 2017

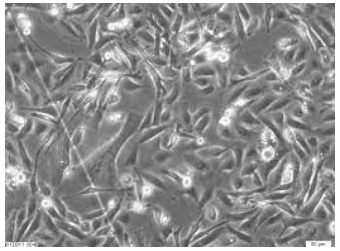
Testování nových kandidátů na léčiva v biologické laboratoři

Group of Doc. Kamil Paruch

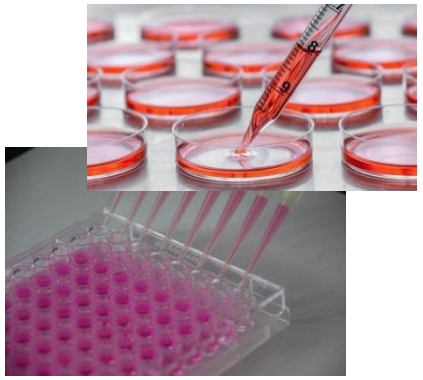
LABORATORY OF ORGANIC SYNTHESIS AND MEDICINAL CHEMISTRY

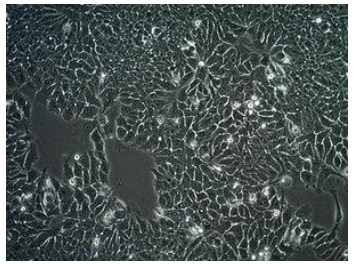
- jsou nové molekuly (kandidáti na inhibitory Haspinu) dostatečně efektivní?
- nejsou pro buňky příliš toxické?
- cílí opravdu Haspin kinázu (jsou dostatečně selektivní)
- který z kandidátu je nejlepší?





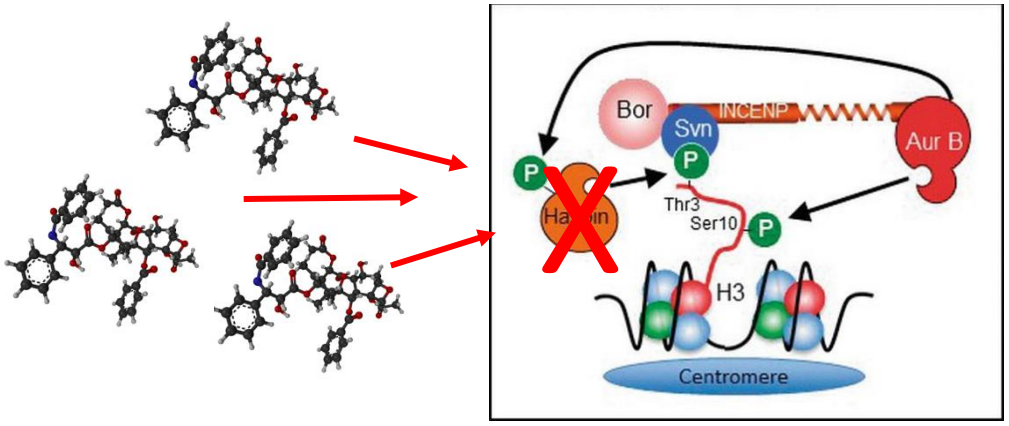
MDA-MB-231
nádorová buněčná linie



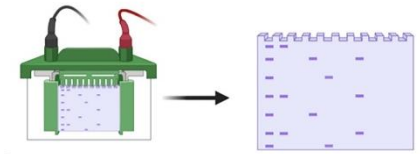


MCF7
nádorová buněčná linie

Testování nových kandidátů na léčiva – příklady experimentů a výsledků

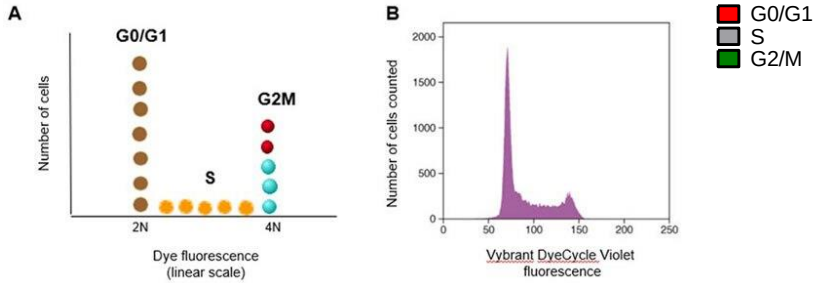


Sledování vlivu inhibitoru kinázy na specifický substrát pH3T3 – western blot



Sledování vlivu na buněčný cyklus (ovlivnění mitózy po inhibici)

Na základě obsahu DNA při průchodu buňky buněčným cyklem pomocí průtokové cytometrie

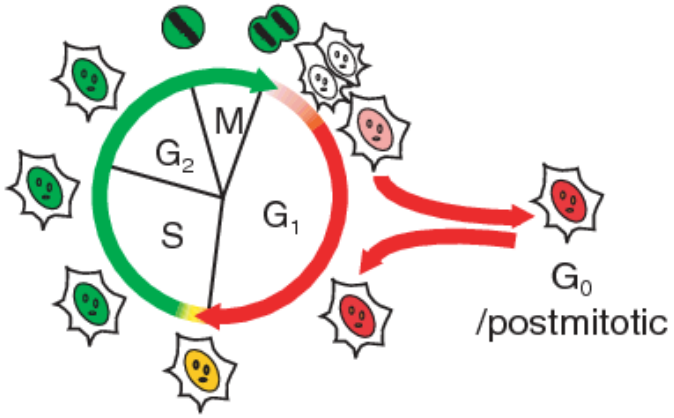


Posouzení efektivity a cytotoxicity jednotlivých nových inhibitorů

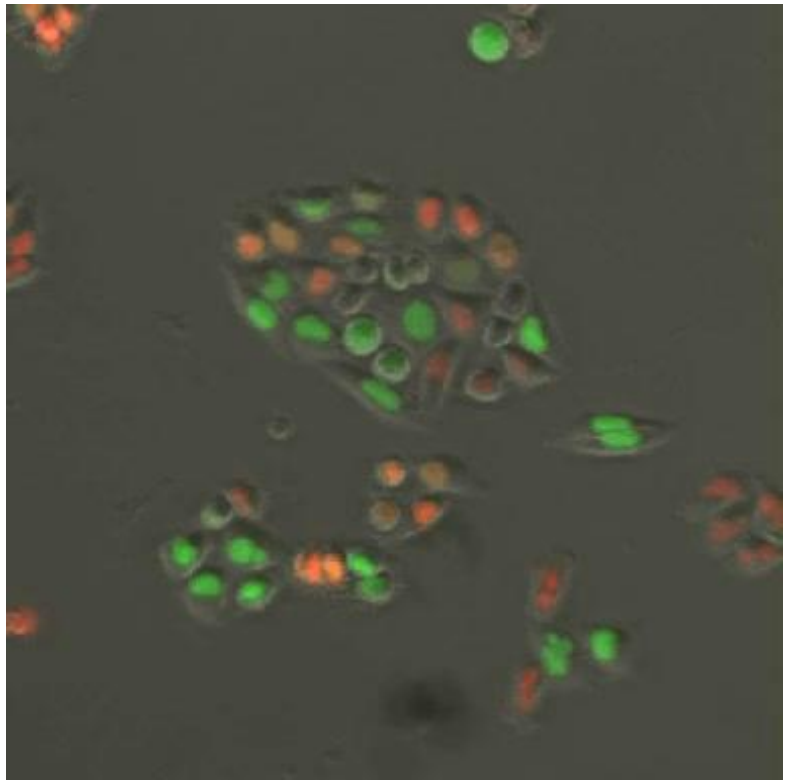
Sledování viablity buněk a odpovědi v závislosti na použité koncentraci (ATP assay)

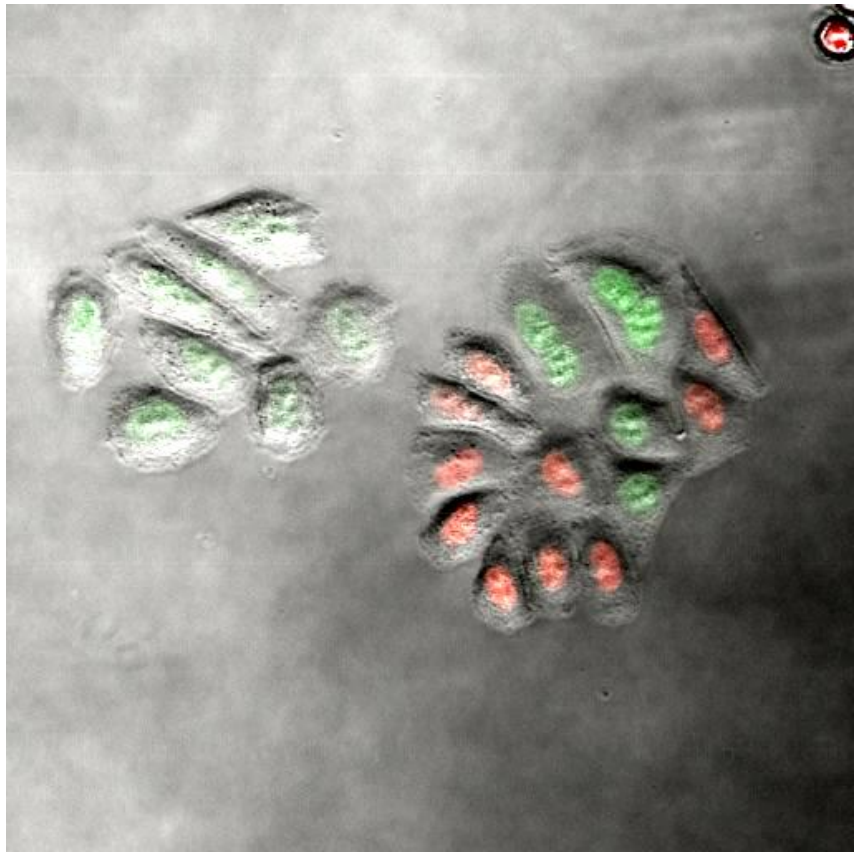
Testování nových kandidátů na léčiva – příklady experimentů a výsledků

„live-imaging“ mikroskopie - sledování vlivu inhibitorů Haspinu online



Kontrolní buňky s Fucci2 reportérem





Buňky s Fucci2 reportérem ovlivněné Haspin inhibitorem

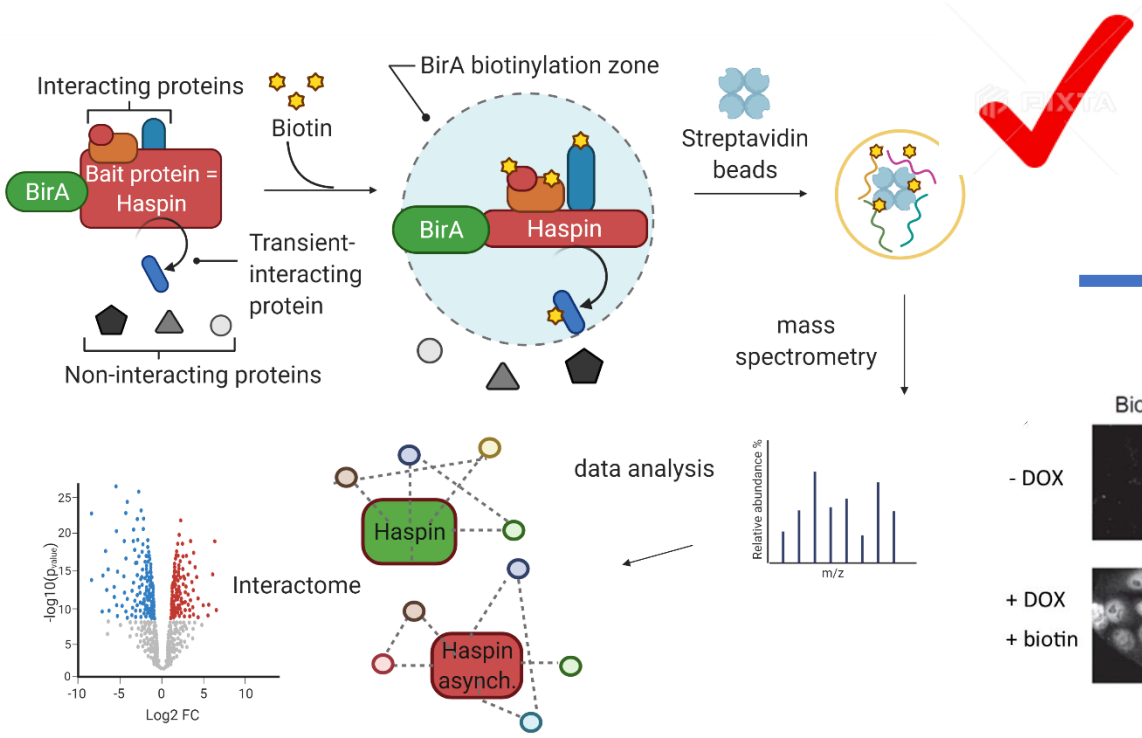
Zaujala tě kináza Haspin?

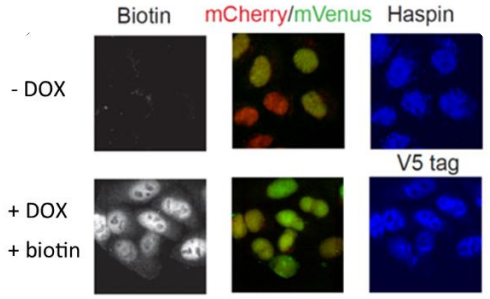
Hledáme motivované studenty pro bakalářský projekt!

Je Haspin pouze nekanonická kináza s jedinou rolí v mitóze?

Nebo může mít i jiné funkce v rámci buněčné plasticity?

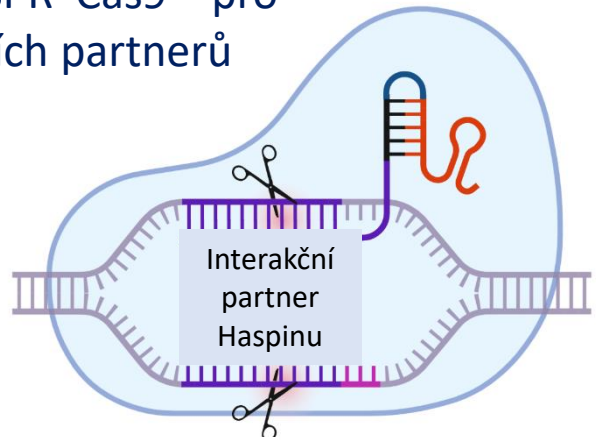
Studium interaktomu Haspinu pomocí metody BioID

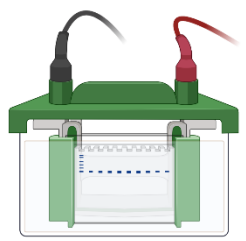


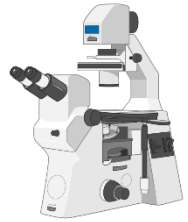


Příprava modifikované buněčné line pomocí CRISPR Cas9 pro validaci interakčních partnerů

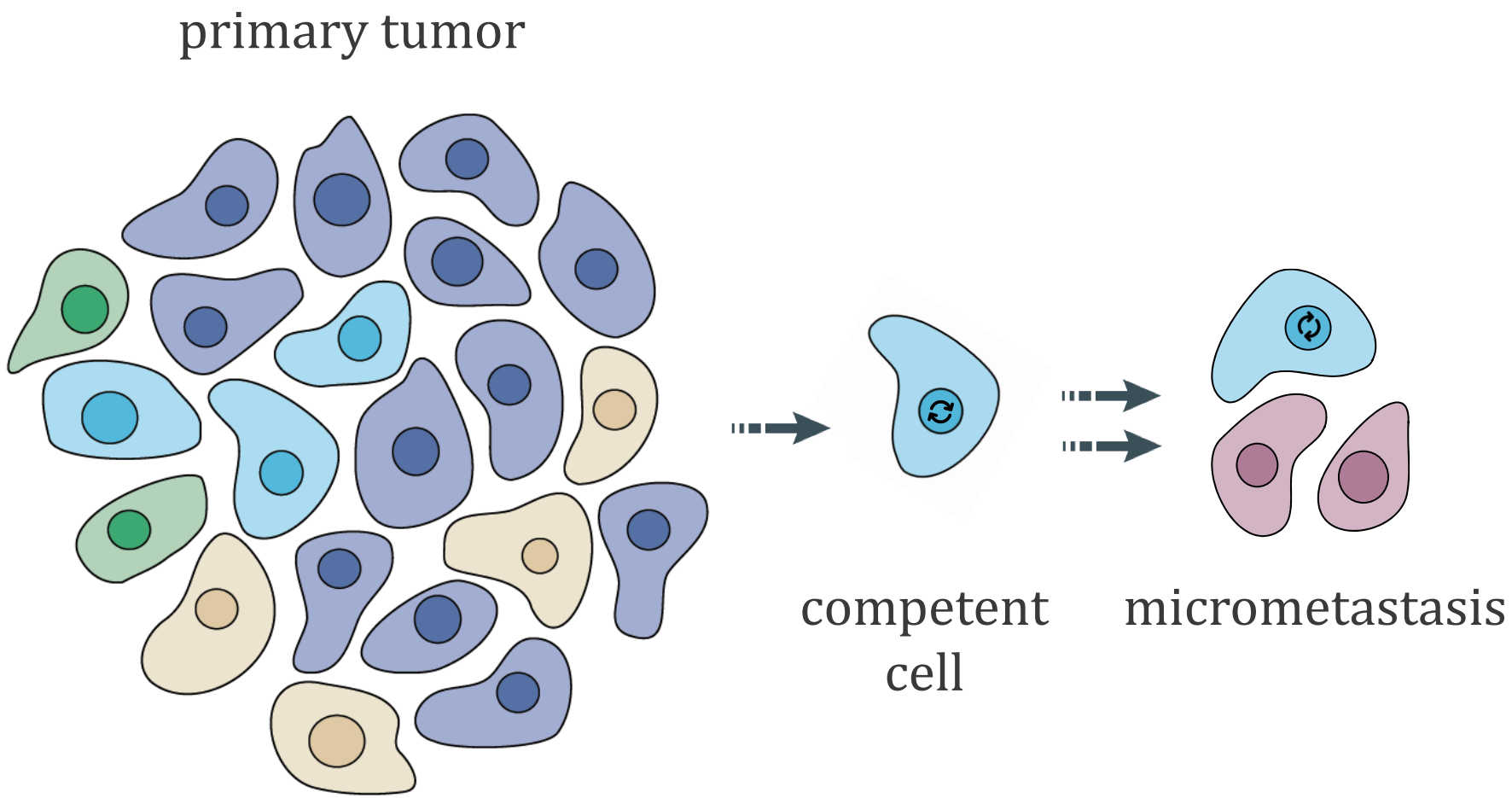
TO - DO







Jaké mechanismy regulují plasticitu buněk?

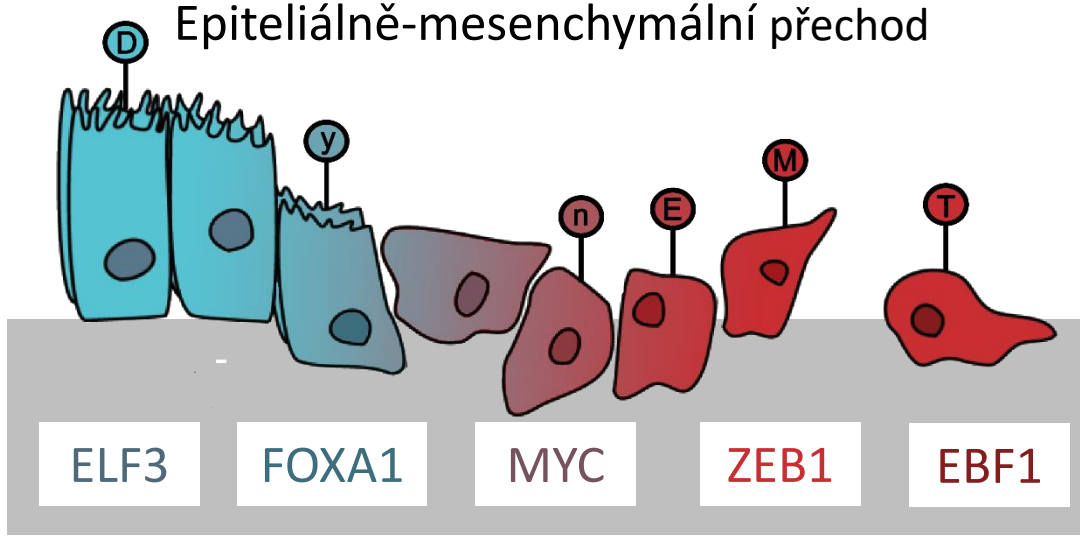


Primární nádor prsu → Metastáze nádoru prsu

Plasticita nádorových buněk

Epiteliálně-mesenchymální přechod

Epitheliální buňka

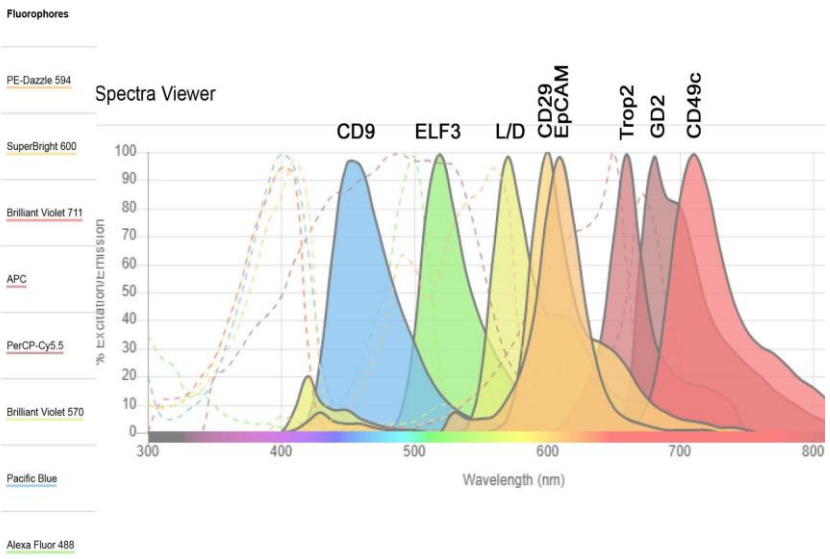


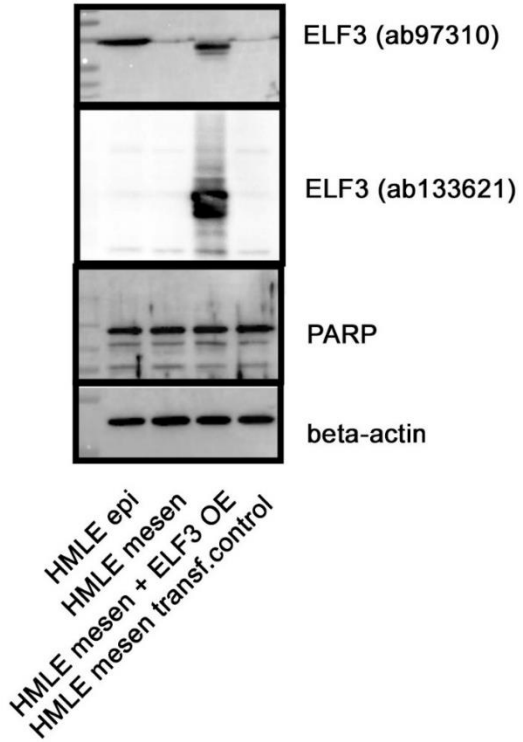
Mesenchymální buňka

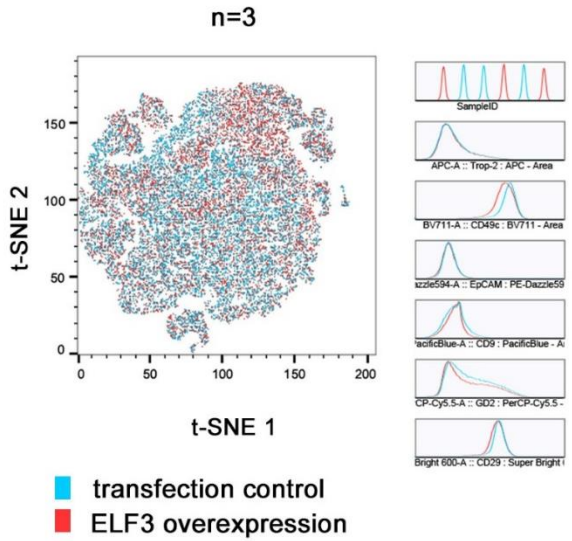
- analýza povrchových molekul epiteliálních a mesenchymálních buněk
- analýza transkripčních faktorů epiteliálních a mesenchymálních buněk
- jaké transkripční faktory řídí regulaci exprese povrchových molekul
- modulací exprese transkripčních faktorů modulovat povrch a fenotyp nádorových buněk

Metody analýzy

1. průtoková cytometrie







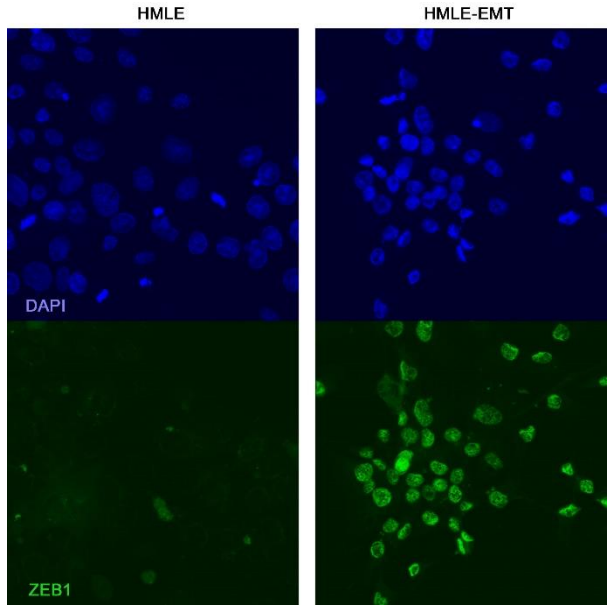
Metody analýzy

2. bioinformatika – analýza vazebných míst

Western blotting – hladina proteinu

PCR- genová exprese

barvení protilátkou – proteinová lokalizace



Epithelial-like

Mesenchymal-like

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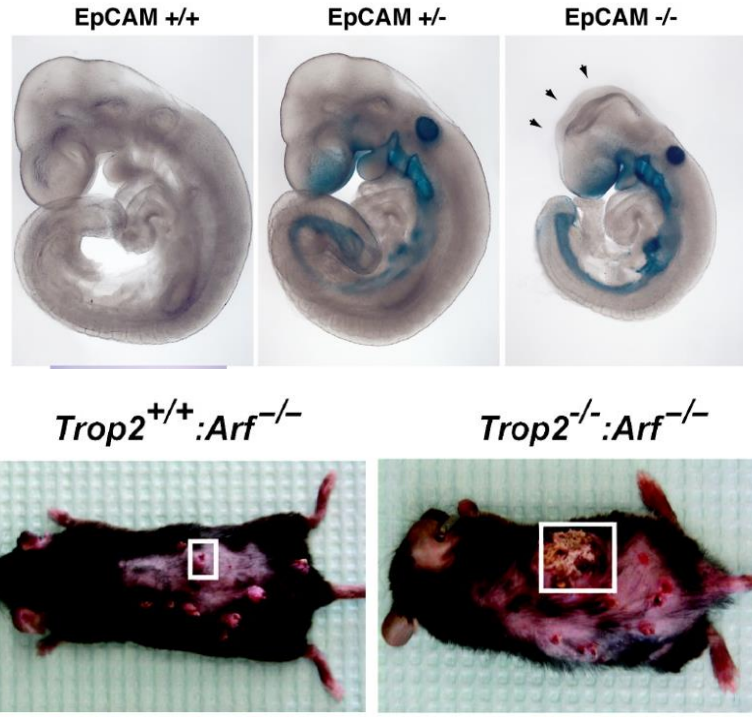
Metody analýzy

3. inducibilní knock-down či ektopická exprese transkripčních faktorů

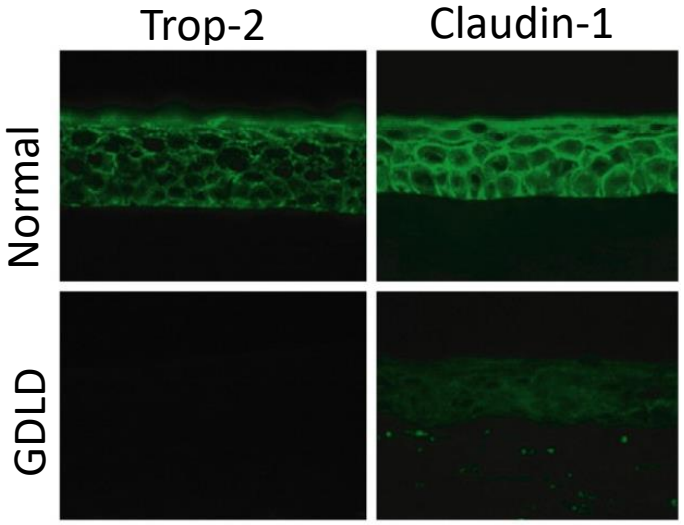
Trop-2 – impact on the tissue organization

- **Homolog of EpCAM**
- high Trop-2 and EpCAM - **stem cell** characteristics, **epithelial progenitors**
- EpCAM loss - lethal vs Trop-2 loss - tumor promotion
- Involvement in organization of epithelium (proper **localization of tight juction proteins Claudins**)



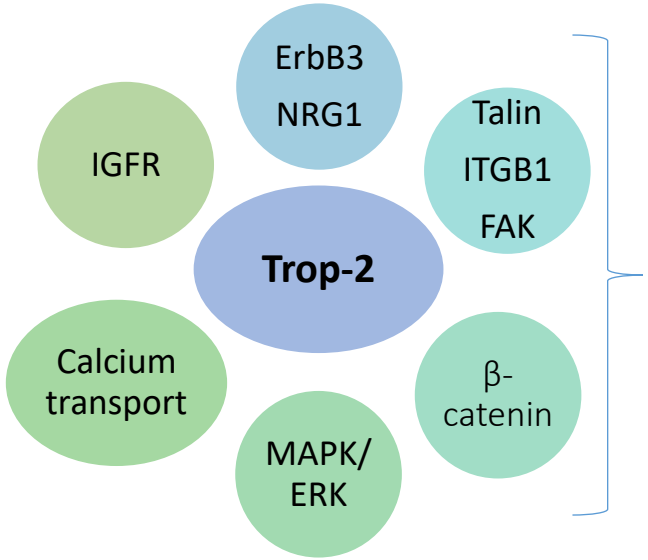
Trop-2 mutation

Gelatinous drop-like corneal dystrophy:



https://www.sciencedirect.com/science/article/pii/S0002944010601885

Possible Trop-2 signaling role in cancer



REPRODUCIBILITY ISSUES … ROLE OF TROP-2 NEEDS TO BE CLARIFIED

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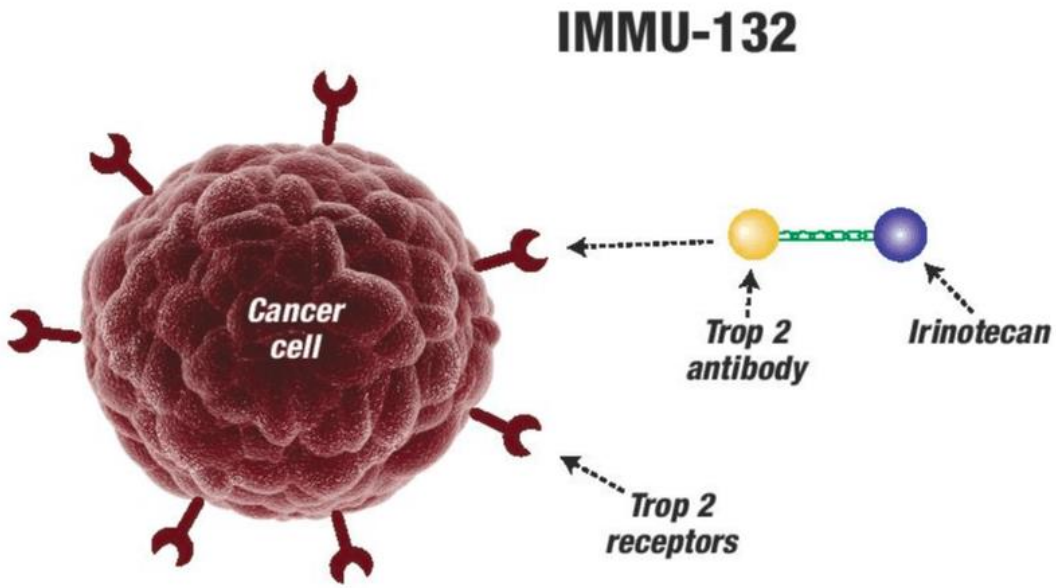
Trop-2
great target for cancer therapy?

- **antibody-based cancer therapy** (metastatic triple negative breast cancer)

sacituzumab govitecan



Trodelvy, SÚKL 3/2022

PROS +

- Trop-2 **overexpressed in many cancers** (breast, prostate,…)
- Association with progenitor and stem cells characterictics
- **Trop-2 stimulates tumour growth**
- Trop-2 drives metastasis (reported for prostate cancer)

Trop-2
great target for cancer therapy?

- **antibody-based cancer therapy** (metastatic triple negative breast cancer)

PROS +

- Trop-2 **overexpressed in many cancers** (breast, prostate,…)
- Association with progenitor and stem cells characterictics
- **Trop-2 stimulates tumour growth**
- Trop-2 drives metastasis (reported for prostate cancer)

CONS -

- **Trop-2 KO in mice** – promotion of **solid tumors development**
- Trop-2 connected with an **epithelial phenotype and is suppressed by EMT** transcription factors
- **Intra- and intertumoral heterogeneity** in Trop-2 expression
- **Favourable effect of Trop-2** high expression in some cancer patients datasets

In vivo phenotype of Trop-2 KO breast cancer cells
(orthotopic model – spontaneous metastasis)

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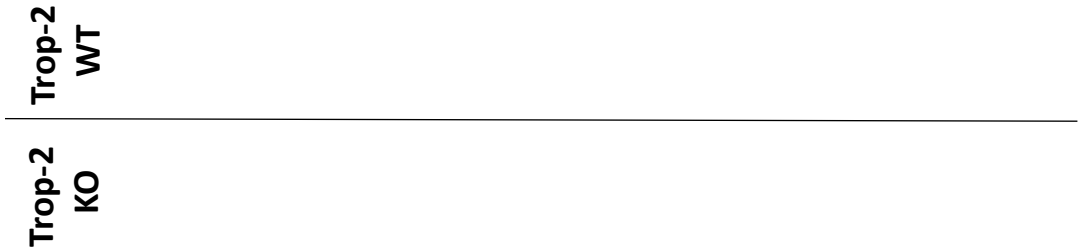
Growth of primary tumor and spontaneous metastasis of breast cancer models:

Growth of primary tumor: 4T1 12B luc2

Lung metastasis: 4T1 12B luc2 (clonnogenic assay)

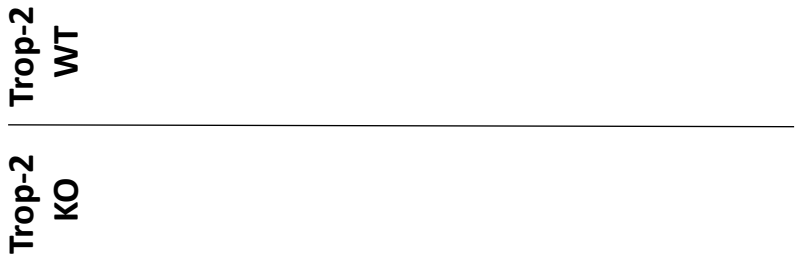
Clonogenic assay quantification



Growth of primary tumor: T-47D

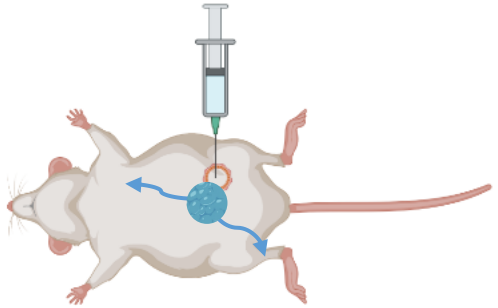
Bone metastasis: T-47D (Ex vivo imaging)

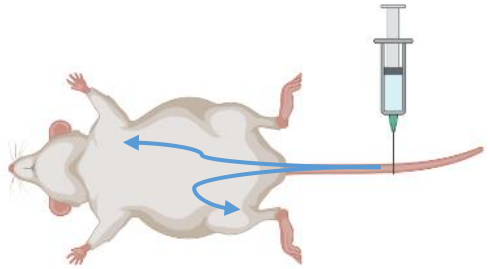
Ex vivo imaging quantification



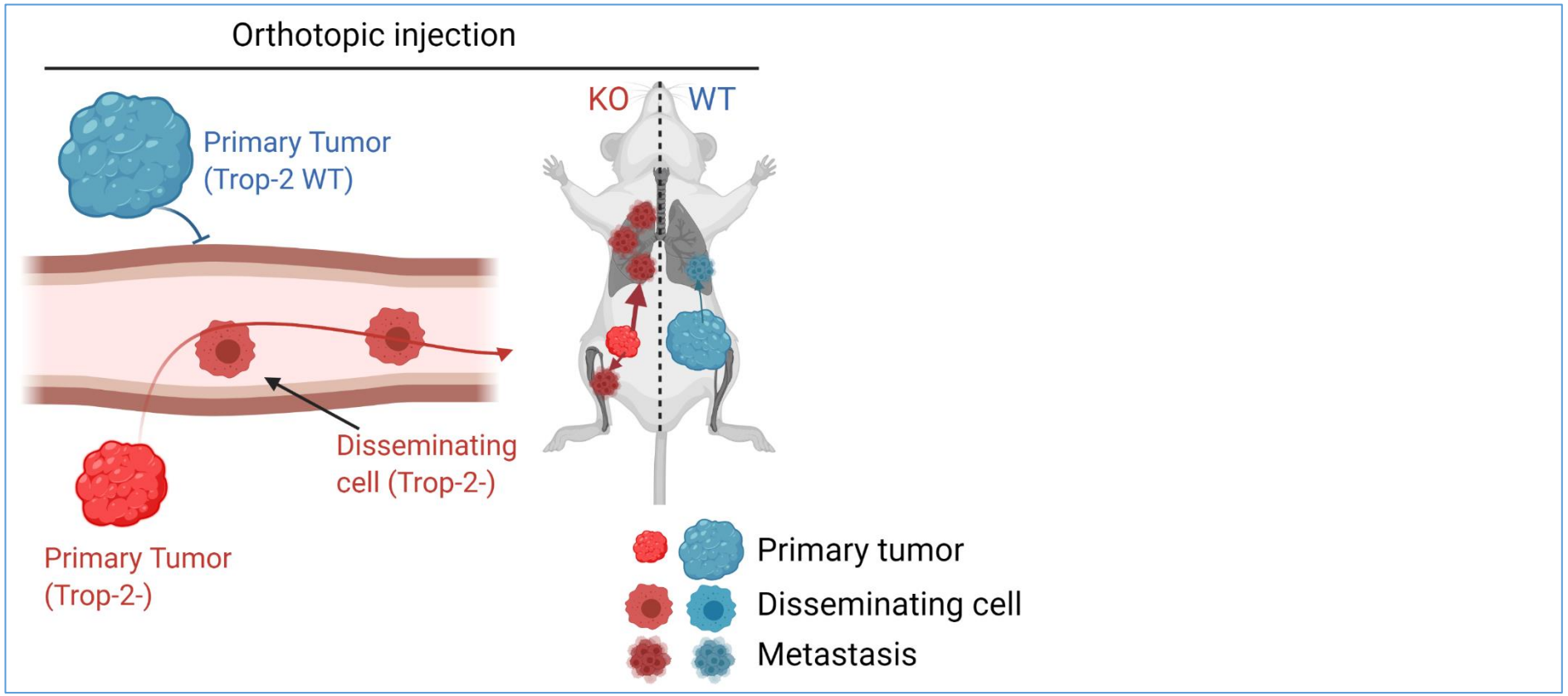
In vivo phenotype of Trop-2 KO breast cancer cells

Spontaneous dissemination
(mammary fat pad injection)



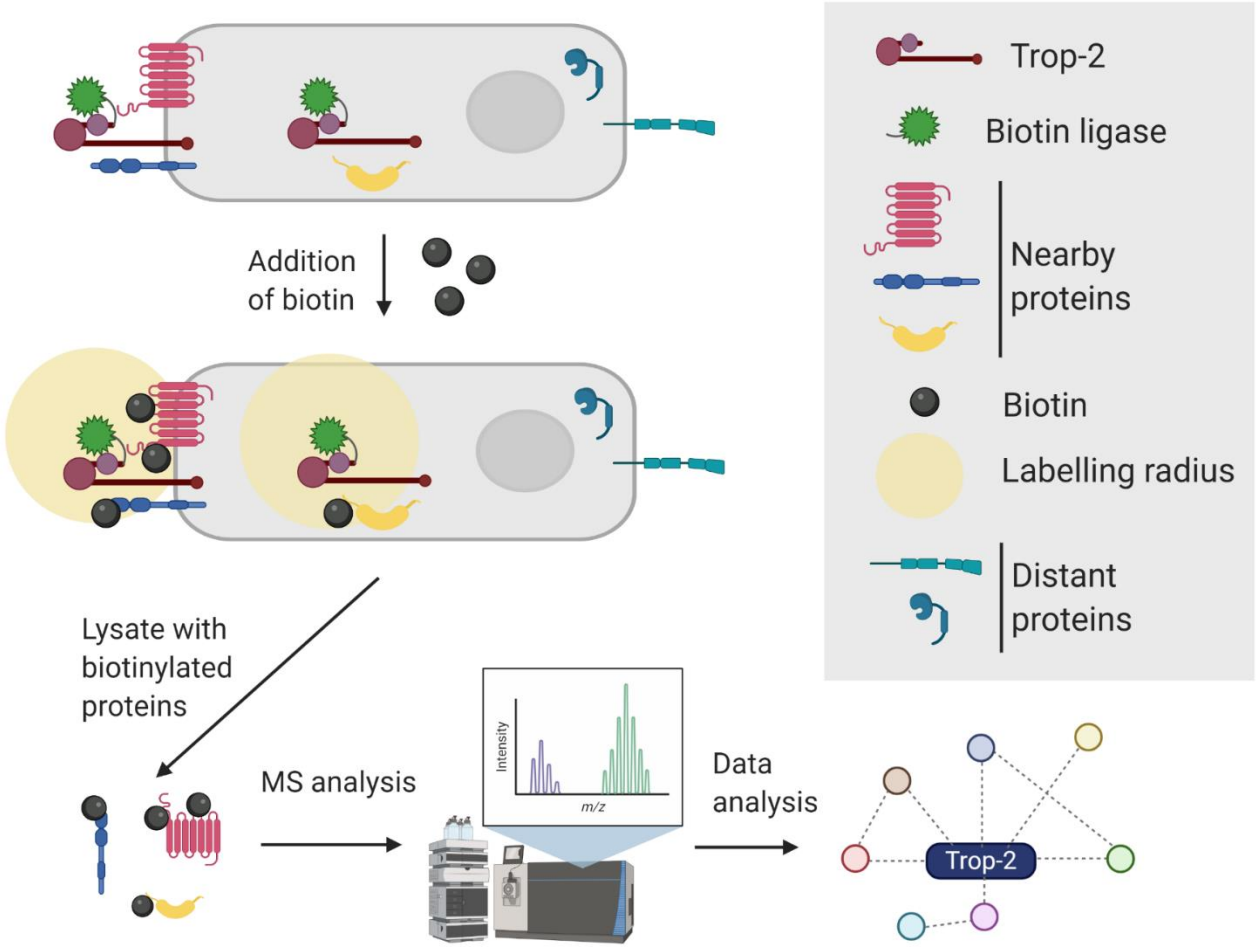


Immediate dissemination
(vein/artery)

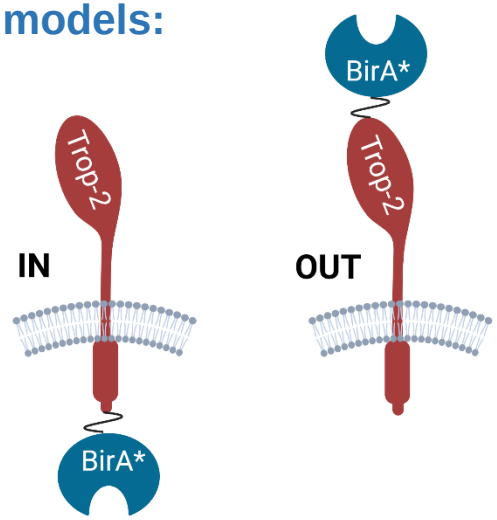


Interactome

Scheme of BioID assay:

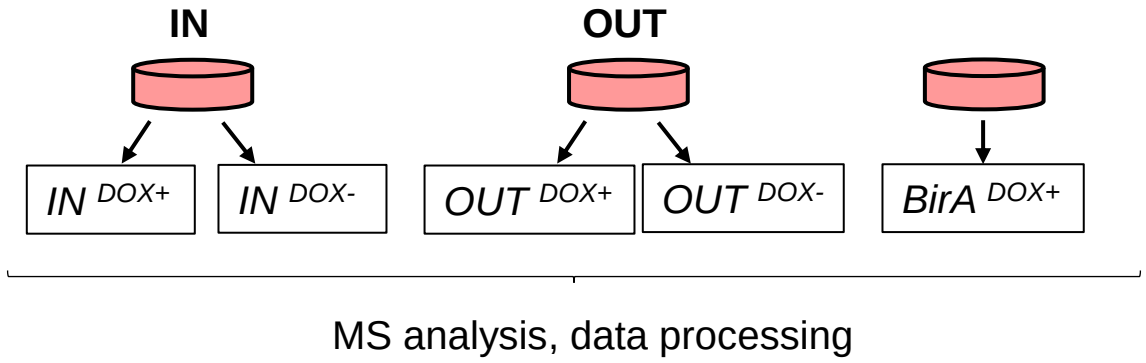


Design of used models:



Design of pulldown for MS:

MDA-MB-231 and HMLE



SOUČEK lab

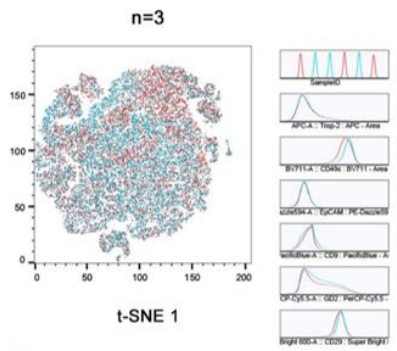
Zaujala tě plasticita nádorových buněk a mechanismy její regulace?

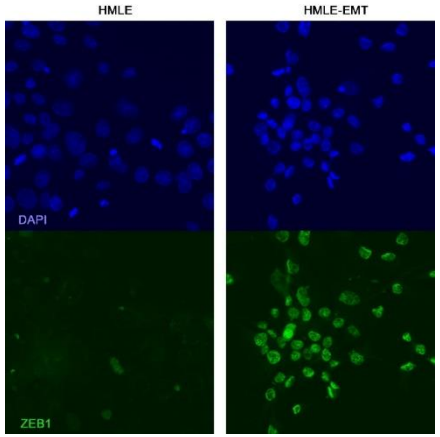
Hledáme motivované studenty pro bakalářský projekt!

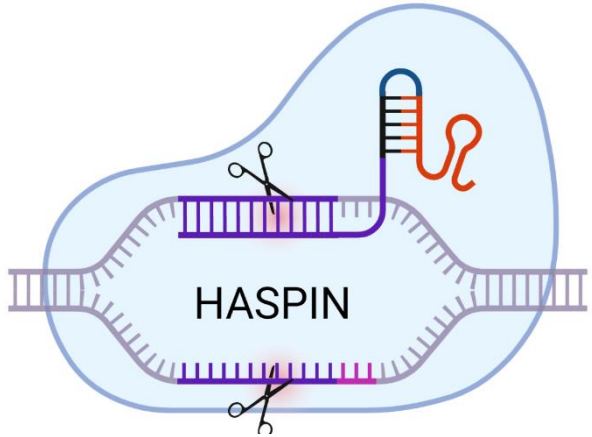
Jakým způsobem je regulována změna exprese povrchových molekul a kontextu zdravého a transformovaného prsního epitelu?

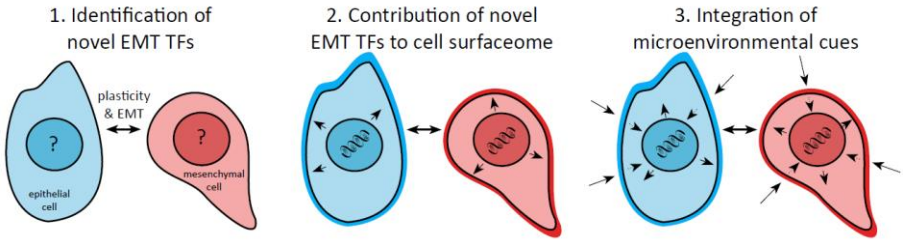
Jakou roli hraje v regulaci plasticity nádorové mikroprostředí?

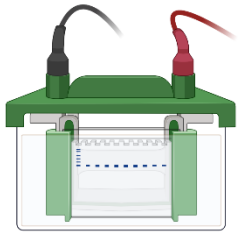
Lze plasticitu nádorových buněk farmakologicky modulovat?

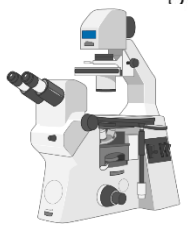












Co nabízíme?

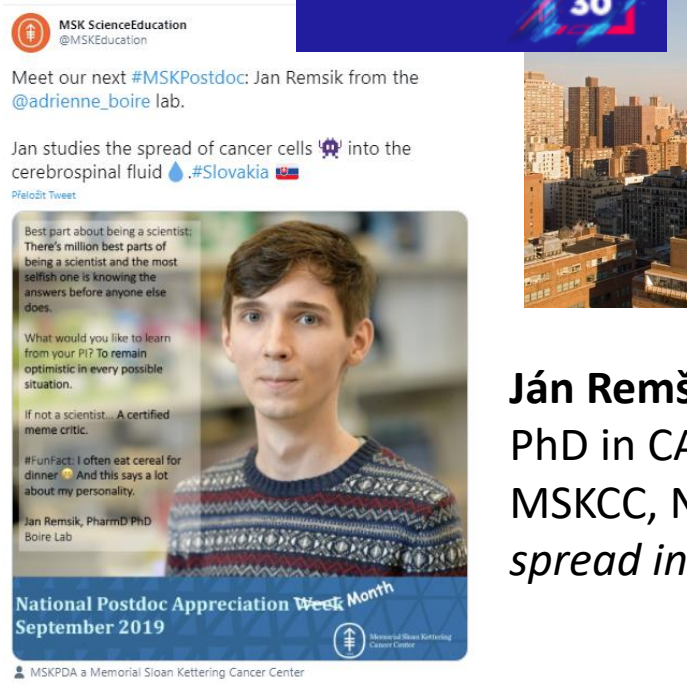
- Experimentální bakalařské práce
- Témata navázaná na výzkumné projekty z oblasti základního a translačního výzkumu
- Široké metodické zázemí od *in vitro, in vivo* a pacientské vzorky

Koho hledáme?

- Zvídavé studenty kteří touží objevovat a nebojí se slepých uliček ☺

SELECTED ALUMNI

Vojtěch Dvořák
MSc in CAP –> PhD student at Ce-M-M, Vienna, *drug resistance*



Ján Remšík
PhD in CAP – > postdoc at MSKCC, NYC, USA, *cancer spread into cerebrospinal fluid*

Stanislav Drápela
PhD in CAP – > postdoc at Moffitt, FL, USA, from 5/2021, *cancer metabolism*

Andrea Staršíchová
MSc in CAP – > PhD at University of Münster European Institute of Molecular Imaging

Partners

FNUSA ICRC
ST. ANNE'S UNIVERSITY HOSPITAL BRNO
INTERNATIONAL CLINICAL RESEARCH CENTER

MUNI

Czech Academy of Sciences

IBP
Institute of Biophysics

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MASARYKŮV ONKOLOGICKÝ ÚSTAV

Univerzita Palackého v Olomouci

FAKULTNÍ NEMOCNICE OLOMOUC

tirol kliniken

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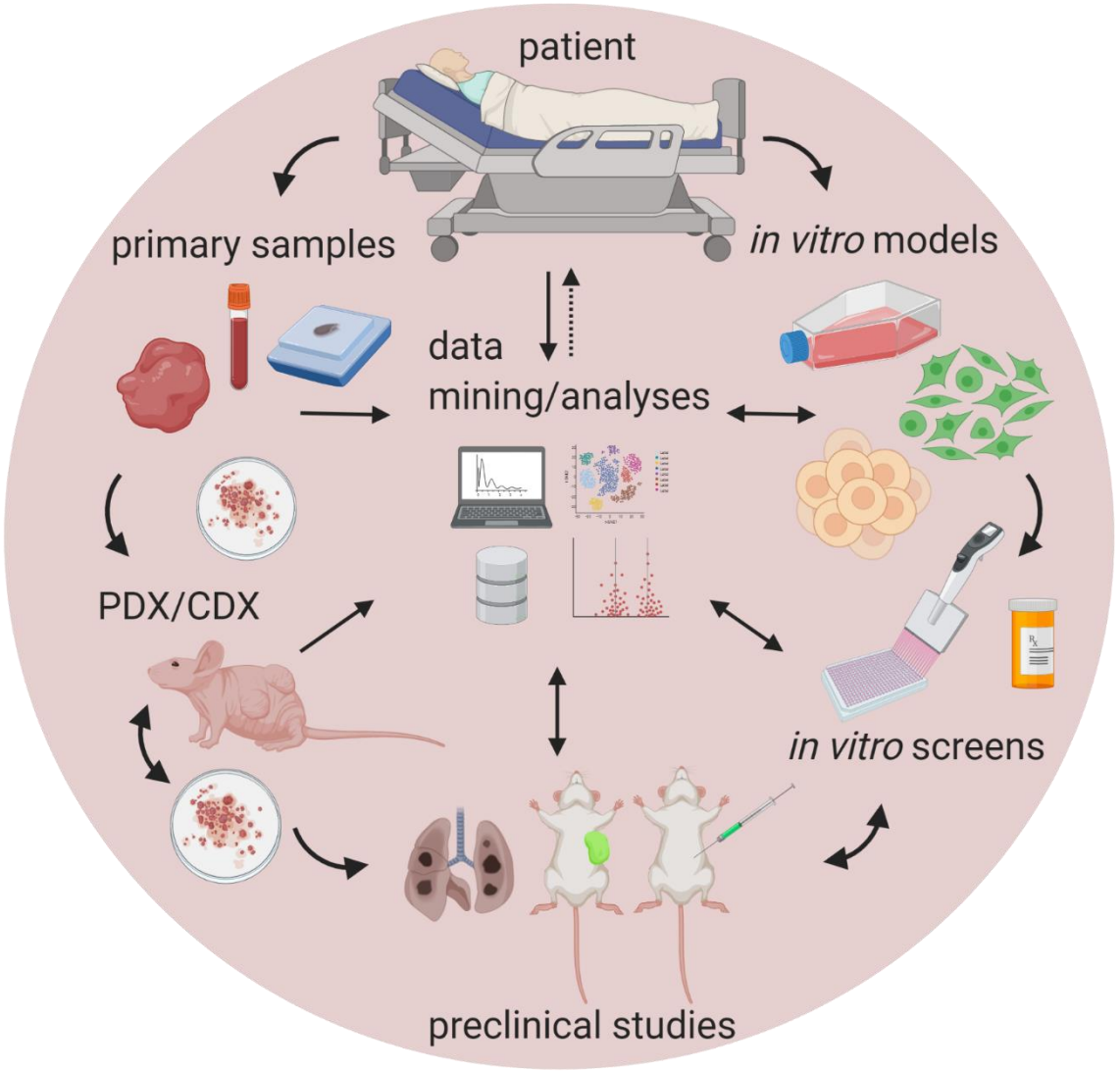
RSM
Erasmus
ERASMUS UNIVERSITY

GAČR
GRANTOVÁ AGENTURA ČESKÉ REPUBLIKY

AZV ČR
AGENTURA PRO ZDRAVOTNICKÝ VÝZKUM ČESKÉ REPUBLIKY

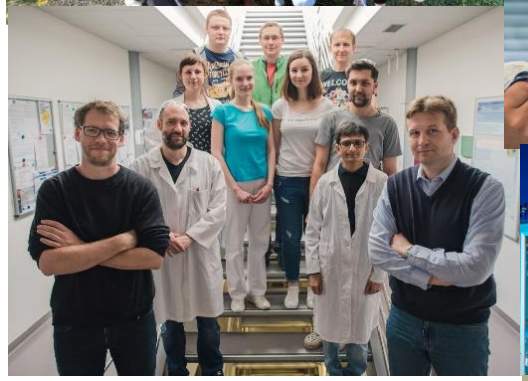


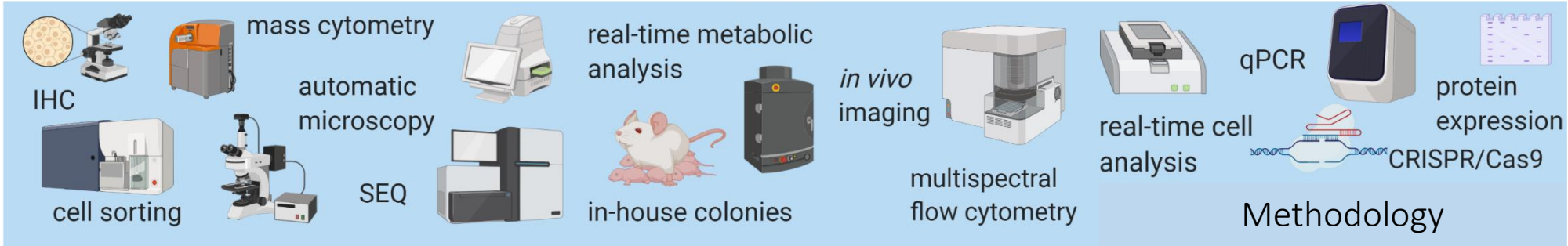
Team & Collaborators







THANK YOU FOR YOUR ATTENTION