CHARLES UNIVERSITY
First Faculty of Medicine
Department BIOCEV
Průmyslová 595, 252 50 Vestec, Czech Republic
Head: Prof. Tomas Stopka MD, PhD

Title: Biomedicine and biotechnology
B90275

Annotation: This subject focuses on educating students in biomedical research and biotechnologies. It teaches the basis of scientific work, introduction to methodology in biomedicine up to the development of novel diagnostics and therapeutics. Lectures and seminars will contain the insight into modern tools such as transgenic biology or global technologies such as OMICs.

Students are encouraged to read education material (available at https://biocev.lf1.cuni.cz/vyuka) ahead of the seminar.

Lectures will be broadcasted online via **Microsoft Teams** (or in BIOCEV / Institute of Anatomy - based on actual pandemic situation). Further information will be sent to all enrolled students by email prior to the first lecture. In case of questions and to enrol, please contact Lucie Vyšatová (lucie.vysatova@lf1.cuni.cz)

Lecture 1 – March 4th, 2021
Prof. Tomáš STOPKA MD, PhD
https://stopka-lab.lf1.cuni.cz/en
Title: **CELL BIOLOGY** : **Stem cell biology versus proliferation and differentiation control**
Regulatory mechanisms in normal cell differentiation including transcription factors and their effector pathways. Biology of stem cells and tissue transplantation. Regulation of cell cycle and its detection.
Study material:

1. Kokavec J, Zikmund T, Savvulidi F, Kulvait V, Edelmann W, Skoultchi AI, Stopka T. The ISWI ATPase Smarca5 (Snf2h) Is Required for Proliferation and Differentiation of Hematopoietic Stem and Progenitor Cells. Stem Cells. 2017. Jun;35(6):1614-1623. doi: 10.1002/stem.2604.
2. Carvajal, L. A., Neriah, D. B., Senecal, A., Benard, L., Thiruthuvanathan, V., Yatsenko, T., … Steidl, U. (2018). Dual inhibition of MDMX and MDM2 as a therapeutic strategy in leukemia. Science Translational Medicine, 10(436), eaao3003. doi:10.1126/scitranslmed.aao3003
3. Yusenko M, Jakobs A, Klempnauer KH. A novel cell-based screening assay for small-molecule MYB inhibitors identifies podophyllotoxins teniposide and etoposide as inhibitors of MYB activity. Sci Rep. 2018 Sep 3;8(1):13159. doi:10.1038/s41598-018-31620-1.
4. Decker S, Zwick A, Khaja Saleem S, Kissel S, Rettig A, Aumann K, Dierks C. Optimized Xenograft Protocol for Chronic Lymphocytic Leukemia Results in High Engraftment Efficiency for All CLL Subgroups. Int J Mol Sci. 2019 Dec 12;20(24).pii: E6277. doi: 10.3390/ijms20246277.
5. Janku F, Angenendt P, Tsimberidou AM, Fu S, Naing A, Falchook GS, Hong DS, Holley VR, Cabrilo G, Wheler JJ, Piha-Paul SA, Zinner RG, Bedikian AY, Overman MJ, Kee BK, Kim KB, Kopetz ES, Luthra R, Diehl F, Meric-Bernstam F, Kurzrock R.Actionable mutations in plasma cell-free DNA in patients with advanced cancers referred for experimental targeted therapies. Oncotarget. 2015 May 20;6(14):12809-21.
6. Behan FM, Iorio F, Picco G, Gonçalves E, Beaver CM, Migliardi G, Santos R, Rao Y, Sassi F, Pinnelli M, Ansari R, Harper S, Jackson DA, McRae R, Pooley R, Wilkinson P, van der Meer D, Dow D, Buser-Doepner C, Bertotti A, Trusolino L,Stronach EA, Saez-Rodriguez J, Yusa K, Garnett MJ. Prioritization of cancer therapeutic targets using CRISPR-Cas9 screens. Nature. 2019 Apr;568(7753):511-516. doi: 10.1038/s41586-019-1103-9.

Lecture 2 - March 18th, 2021

Prof. MUDr. Karel Smetana, DrSc.

https://skin-stem-cell.webnode.cz/

Title: CELL BIOLOGY : Tumor ecosystem

Role of cancer microenvironment in the control of tumor biology including metastazation. Cancer-associated fibroblasts.

Study material:

1. Dvořánková B, Szabo P, Kodet O, Strnad H, Kolář M, Lacina L, Krejčí E, Naňka O, Šedo A, Smetana K Jr. Intercellular crosstalk in human malignant melanoma. Protoplasma. 2017 May;254(3):1143-1150. doi: 10.1007/s00709-016-1038-z.
2. Lacina L, Plzak J, Kodet O, Szabo P, Chovanec M, Dvorankova B, Smetana K Jr.Cancer Microenvironment: What Can We Learn from the Stem Cell Niche. Int J Mol Sci. 2015 Oct 12;16(10):24094-110. doi: 10.3390/ijms161024094.
3. Plzák J, Bouček J, Bandúrová V, Kolář M, Hradilová M, Szabo P, Lacina L, Chovanec M, Smetana K Jr. The Head and Neck Squamous Cell Carcinoma Microenvironment as a Potential Target for Cancer Therapy.
4. Cancers (Basel). 2019 Mar 28;11(4). pii: E440. doi: 10.3390/cancers11040440.

Lecture 3 – April 1st, 2021

MUDr. Ondřej Havránek, PhD

https://biocev.lf1.cuni.cz/havranek-lab

Title: GENETICS : Cancer genomes and genome editing technology

Cancer associated acquired DNA mutations and their role in tumor development, progression, and therapy resistance. Consequences for interaction of tumor cells with immune system. Use of genome modifying technologies to create models for cancer research and options for therapy.

Study material:

1. Stratton M.R., Campbell P. J., Futreal P.A., The cancer genome. Nature. Vol.458/9 April 2009. Doi:10.1038/nature07943.
2. Ding L, Bailey MH, Porta-Pardo E, Thorsson V, Colaprico A, Bertrand D, Gibbs DL, Weerasinghe A, Huang KL, Tokheim C, Cortés-Ciriano I, Jayasinghe R, Chen F,Yu L, Sun S, Olsen C, Kim J, Taylor AM, Cherniack AD, Akbani R, Suphavilai C,Nagarajan N, Stuart JM, Mills GB, Wyczalkowski MA, Vincent BG, Hutter CM,Zenklusen JC, Hoadley KA, Wendl MC, Shmulevich L, Lazar AJ, Wheeler DA, Getz G;Cancer Genome Atlas Research Network. Perspective on Oncogenic Processes at the End of the Beginning of Cancer Genomics. Cell. 2018 Apr 5;173(2):305-320.e10.doi: 10.1016/j.cell.2018.03.033.
3. Sanchez-Vega F, Mina M, Armenia J, Chatila WK, Luna A, La KC, Dimitriadoy S, Liu DL, Kantheti HS, Saghafinia S, Chakravarty D, Daian F, Gao Q, Bailey MH,Liang WW, Foltz SM, Shmulevich I, Ding L, Heins Z, Ochoa A, Gross B, Gao J, Zhang H, Kundra R, Kandoth C, Bahceci I, Dervishi L, Dogrusoz U, Zhou W, Shen H, Laird PW, Way GP, Greene CS, Liang H, Xiao Y, Wang C, Iavarone A, Berger AH, Bivona TG,Lazar AJ, Hammer GD, Giordano T, Kwong LN, McArthur G, Huang C, Tward AD,Frederick MJ, McCormick F, Meyerson M; Cancer Genome Atlas Research Network, Van Allen EM, Cherniack AD, Ciriello G, Sander C, Schultz N. Oncogenic Signaling Pathways in The Cancer Genome Atlas. Cell. 2018 Apr 5;173(2):321-337.e10. doi:10.1016/j.cell.2018.03.035.
4. Kebriaei P, Izsvák Z, Narayanavari SA, Singh H, Ivics Z. Gene Therapy with the Sleeping Beauty Transposon System. Trends Genet. 2017 Nov;33(11):852-870. doi:10.1016/j.tig.2017.08.008.
5. Hsu PD,Lander ES,Zhang F. Development and Applications of CRISPR-Cas9 for Genome Engineering. Cell 157, June 5, 2014. doi:10.1016/j.cell.2014.05.010.
6. Komor AC, Badran AH, Liu DR. CRISPR-Based Technologies for the Manipulation of Eukaryotic Genomes. Cell. 2017 Apr 20;169(3):559. doi:10.1016/j.cell.2017.04.005.
7. Barrangou R, Doudna JA. Applications of CRISPR technologies in research and beyond. Nat Biotechnol. 2016;34(9):933-941. doi: 10.1038/nbt.3659.
8. Hoadley KA, Yau C, Hinoue T, Wolf DM, Lazar AJ, Drill E, Shen R, Taylor AM,Cherniack AD, Thorsson V, Akbani R, Bowlby R, Wong CK, Wiznerowicz M, Sanchez-Vega F, Robertson AG, Schneider BG, Lawrence MS, Noushmehr H, Malta TM;Cancer Genome Atlas Network, Stuart JM, Benz CC, Laird PW. Cell-of-Origin Patterns Dominate the Molecular Classification of 10,000 Tumors from 33 Types of Cancer. Cell. 2018 Apr 5;173(2):291-304.e6. doi: 10.1016/j.cell.2018.03.022.
9. June CH, O'Connor RS, Kawalekar OU, Ghassemi S, Milone MC. CAR T cell immunotherapy for human cancer. Science. 2018 Mar 23;359(6382):1361-1365. doi:10.1126/science.aar6711.

10. Bailey MH, Tokheim C, Porta-Pardo E, Sengupta S, Bertrand D, Weerasinghe A, Colaprico A, Wendl MC, Kim J, Reardon B, Kwok-Shing Ng P, Jeong KJ, Cao S, Wang Z, Gao J, Gao Q, Wang F, Liu EM, Mularoni L, Rubio-Perez C, Nagarajan N, Cortés-Ciriano I, Zhou DC, Liang WW, Hess JM, Yellapantula VD, Tamborero D, Gonzalez-Perez A, Suphavilai C, Ko JY, Khurana E, Park PJ, Van Allen EM, Liang H; MC3 Working Group; Cancer Genome Atlas Research Network, Lawrence MS, Godzik A, Lopez-Bigas N, Stuart J, Wheeler D, Getz G, Chen K, Lazar AJ, Mills GB, Karchin R, Ding L. Comprehensive Characterization of Cancer Driver Genes and Mutations. Cell. 2018 Aug 9;174(4):1034-1035. doi: 10.1016/j.cell.2018.07.034.

Lecture 4 – April 15th, 2021

Ing. Ľubica Ďuďáková, Ph.D.

Title: **Molecular techniques and methods for mutation detection and screening of human diseases** - In the past decade, sequencing technology has evolved rapidly with the advent of high-throughput next generation sequencing. By adopting and leveraging next generation sequencing, clinical laboratories are now performing an ever increasing catalogue of genetic testing that has been accompanied by new challenges in sequence interpretation. This lecture is focused on how to interpret sequence variants and to ascertain the clinical significance using criteria of ACMG (American College of Medical Genetics) standards.

Study material:

1. Ogino S, Gulley ML, den Dunnen JT, Wilson RB; Association for Molecular Pathology Training and Education Committtee. Standard mutation nomenclature in molecular diagnostics: practical and educational challenges [published correction appears in J Mol Diagn. 2009 Sep 1;11(5):494]. *J Mol Diagn*. 2007;9(1):1-6. doi:10.2353/jmoldx.2007.060081
2. Richards CS, Bale S, Bellissimo DB, Das S, Grody WW, Hegde MR, Lyon E, Ward BE; Molecular Subcommittee of the ACMG Laboratory Quality Assurance Committee. ACMG recommendations for standards for interpretation and reporting of sequence variations: Revisions 2007. Genet Med. 2008 Apr;10(4):294-300. doi: 10.1097/GIM.0b013e31816b5cae.
3. Richards S, Aziz N, Bale S, et al. Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. *Genet Med*. 2015;17(5):405-424. doi:10.1038/gim.2015.30

Lecture 5– April 29th, 2021

Assoc. Prof. RNDr. Jiří Petrák, PhD

https://faustus-technologies.webnode.cz/

Title: **CLINICAL PROTEOMICS**

Using efficient separation methods and high-resolution mass spectrometry PROTEOMICS enables monitoring of quantitative and qualitative changes of thousands of proteins in biological samples. Detailed knowledge of proteome changes in cells and tissues can elucidate molecular mechanisms of physiologic and pathologic processes, and identify disease markers or novel therapeutic targets.

Study material:

1. O'Neill J.R. (2019) An Overview of Mass Spectrometry-Based Methods for Functional Proteomics. In: Wang X., Kuruc M. (eds) Functional Proteomics. Methods in Molecular Biology, vol 1871. Humana Press, New York, NY
2. Domon, B. (2006). Mass Spectrometry and Protein Analysis. Science, 312(5771), 212–217. doi:10.1126/science.1124619

Lecture 6 – May 13th, 2021

Mgr. Peter Dráber, PhD

https://biocev.lf1.cuni.cz/draber-laboratory

Title: **The role of cell death in tissue homeostasis and autoimmune disorders**

Cell death is necessary for removal of damaged cells and tissue renewal. However, aberrant cell death can lead to severe autoimmune disorders. The molecular pathways triggering cell death in physiological settings and pathological conditions will be discussed.

Study material:

1. Lafont E, Draber P, Rieser E, Reichert M, Kupka S, de Miguel D, Draberova H, von Mässenhausen A, Bhamra A, Henderson S, Wojdyla K, Chalk A, Surinova S, Linkermann A, Walczak H. TBK1 and IKKε prevent TNF-induced cell death by RIPK1 phosphorylation. Nat Cell Biol. 2018 Dec;20(12):1389-1399. doi: 10.1038/s41556-018-0229-6.

2. Newton K, Wickliffe KE, Dugger DL, Maltzman A, Roose-Girma M, Dohse M, Kőműves L, Webster JD, Dixit VM. Cleavage of RIPK1 by caspase-8 is crucial for limiting apoptosis and necroptosis. Nature. 2019 Oct;574(7778):428-431. doi: 10.1038/s41586-019-1548-x.
3. Lalaoui N, Boyden SE, Oda H, Wood GM, Stone DL, Chau D, Liu L, Stoffels M, Kratina T, Lawlor KE, Zaal KJM, Hoffmann PM, Etemadi N, Shield-Artin K, Biben C, Tsai WL, Blake MD, Kuehn HS, Yang D, Anderton H, Silke N, Wachsmuth L, Zheng L,Moura NS, Beck DB, Gutierrez-Cruz G, Ombrello AK, Pinto-Patarroyo GP, Kueh AJ,Herold MJ, Hall C, Wang H, Chae JJ, Dmitrieva NI, McKenzie M, Light A, Barham BK,Jones A, Romeo TM, Zhou Q, Aksentijevich I, Mullikin JC, Gross AJ, Shum AK,Hawkins ED, Masters SL, Lenardo MJ, Boehm M, Rosenzweig SD, Pasparakis M, Voss AK, Gadina M, Kastner DL, Silke J. Mutations that prevent caspase cleavage of RIPK1 cause autoinflammatory disease. Nature. 2020 Jan;577(7788):103-108. doi:10.1038/s41586-019-1828-5.

Lecture 7 – May 27th, 2021

Mgr. Miroslav Hons, PhD

https://biocev.lf1.cuni.cz/hons-lab

Title: **Leukocyte migration and immunology**

Migration of leukocytes in healthy and pathological states. Imaging of leukocyte behaviour and interactions. Cell biology of leukocyte motility.

Study material:

1. Pittet MJ, Garris CS, Arlauckas SP, Weissleder R. Recording the wild lives of immune cells. Sci Immunol. 2018 Sep 7;3(27). pii: eaaq0491. doi:10.1126/sciimmunol.aaq0491.
2. Miller, M. J. (2002). Two-Photon Imaging of Lymphocyte Motility and Antigen Response in Intact Lymph Node. Science, 296(5574), 1869–1873. doi:10.1126/science.1070051
3. Mempel, T. R., Henrickson, S. E., & von Andrian, U. H. (2004). T-cell priming by dendriticcells in lymph nodes occurs in three distinct phases. Nature, 427(6970), 154–159. doi:10.1038/nature02238