PRACTICAL LESSONS WITH PRESENTATIONS OF STUDENTS- SUMMER SEMESTER, week 9

1. **Membrane transport (proton pump, Wilson's disease, cystic fibrosis). Protein folding, ubiquitin proteasome system (misfolding diseases, chaperones, defects of the ubiquitin-proteasome- VHL, parkin, HPV induced cancerogenesis).**

   Whom to contact – MUDr. Petr Bušek, Ph.D.

Literature that is to be studied by ALL STUDENTS attending the seminar:

*** Transport** *Harper's Biochemistry, 30th ed, chapter 40- Membranes: Structure and Function*

*** Protein folding, chaperones, proteasome** *Harper's Biochemistry, 30th ed, chapter 49- pp 618-620*

In addition, 6 students will prepare a presentation on one of the topics below. Recommended literature is listed for each of the topics separately. Up to 2 points (which will be added to the points gained in the tests) can be obtained for high quality presentations. Maximum points obtained in this way are 2 per semester.

Case 1- A proton pump (H^+K^+ ATPase)

Aim: to demonstrate the molecular mechanism underlying HCl secretion and how it can be therapeutically influenced

Literature- selected parts from

Shin, J.M. and G. Sachs, *Pharmacology of proton pump inhibitors.* Curr Gastroenterol Rep, 2008. **10**(6): p. 528-34.

Shin, J.M., et al., *The gastric HK-ATPase: structure, function, and inhibition.* Pflugers Arch, 2009. **457**(3): p. 609-22.

Case 2 The role of membrane transporters in the copper metabolism, Wilson's disease

Aim: to demonstrate the pathogenetic role of membrane transporters in the pathogenesis of diseases

Literature

de Bie, P., et al., *Molecular pathogenesis of Wilson and Menkes disease: correlation of mutations with molecular defects and disease phenotypes.* J Med Genet, 2007. **44**(11): p. 673-88.

Case 3 CFTR and cystic fibrosis

Aim: to demonstrate the clinical importance of membrane transport, molecular consequences of mutations affecting proteins and possibilities of therapeutic interventions.

Literature:

Kunzelmann, K. and M. Mall, *Pharmacotherapy of the ion transport defect in cystic fibrosis.* Clin Exp Pharmacol Physiol, 2001. **28**(11): p. 857-67.

Ko, Y.H. and P.L. Pedersen, *Frontiers in research on cystic fibrosis: understanding its molecular and chemical basis and relationship to the pathogenesis of the disease.* J Bioenerg Biomembr, 1997. **29**(5): p. 417-27.

Cheung, J.C. and C.M. Deber, *Misfolding of the cystic fibrosis transmembrane conductance regulator and disease.* Biochemistry, 2008. **47**(6): p. 1465-73.

Case 4 Neurodegenerative diseases and protein aggregation and misfolding- m. Alzheimer, m. Parkinson

Aim: to demonstrate the genesis of „protein misfolding diseases"

Goedert, M., *NEURODEGENERATION. Alzheimer's and Parkinson's diseases: The prion concept in relation to assembled Abeta, tau, and alpha-synuclein.* Science, 2015. **349**(6248): p. 1255555.

Case 5: Molecular chaperones

Aim: to demonstrate the role of molecular chaperones in protein folding

Hartl FU, Hayer-Hartl M. Molecular chaperones in the cytosol: From nascent chain to folded protein. Science 2002; 295: 1852-1858.

Devlin Textbook of Biochemistry with Clinical Correlations, 7th edition pp 116

Case 6 The ubiquitin-proteasome system and human diseases- VHL, parkin, HPV induced cancerogenesis, UPS in cancer treatment

Aim: to demonstrate the role of ubiquitin proteasome system in the pathogenesis of diseases

Reinstein, E. and A. Ciechanover, *Narrative review: protein degradation and human diseases: the ubiquitin connection.* Ann Intern Med, 2006. **145**(9): p. 676-8