האוניברסיטה העברית בירושלים
THE HEBREW UNIVERSITY OF JERUSALEM

Syllabus

Developmental Genetic Basis of Human Disease - 94921

Last update 05-05-2024

HU Credits: *3*

Responsible Department: *Bio-Medical Sciences*

Academic year: *0*

Semester: *2nd Semester*

Teaching Languages: *English*

Campus: *Ein Karem*

Course/Module Coordinator: *Abraham Fainsod*

Coordinator Email: *abraham.fainsod@mail.huji.ac.il*

Coordinator Office Hours:

Teaching Staff:
Prof Abraham Fainsod,
Prof Offer Gerlitz,
Prof Joel Yisraeli,
Prof Ayal Ben-Zvi,

Prof Dan Ben Zvi

Course/Module description:
The developmental basis of human disease - selected subjects

Course/Module aims:
Understand processes in embryonic development that can lead to diseases in the adult

Learning outcomes - On successful completion of this module, students should be able to:
Understand basic developmental processes

Attendance requirements(%):
90

Teaching arrangement and method of instruction: Lectures and guided article reading

Course/Module Content:
Week #1 May 6
9:15-12:00 Offer Gerlitz (A. Fainsod)
Ovarian development and dysgenesis: from Humans to Flies and Back

Project paper:
Zhang S., Huang B., Su P., Chang Q., Li P., Song A., et al. Concentrated exosomes from menstrual blood-derived stromal cells improves ovarian activity in a rat model of premature ovarian insufficiency. Stem Cell Res Ther. 2021 Mar 12;12(1):178. doi: 10.1186/s13287-021-02255-3.

Week #2 May 20
9:15-10:00 Offer Gerlitz (J. Yisraeli)
Reading paper:
Weinberg-Shukron, A., Rachmiel, M., Renbaum, P., Gulsuner, S., Walsh, T., Lobel, O., Dreifuss, A., Ben-Moshe, A., Zeligson, S., Segel, R., Shore, T., Kalifa, R., Goldberg, M., King, M.-C., Gerlitz, O., Levy-Lahad, E., Zangen, D., 2018. Essential role of BRCA2 in ovarian development and function. N. Engl. J. Med. 379, 1042□1049. doi:10.1056/NEJMoa1800024

10:15-12:00 Joel Yisraeli (O. Gerlitz)
Primary cilia and Ciliopathies

Project paper:
Katoh TA, Omori T, Mizuno K, Sai X, Minegishi K, Ikawa Y, Nishimura H, Itabashi T, Kajikawa E, Hiver S, Iwane AH, Ishikawa T, Okada Y, Nishizaka T, Hamada H. Immotile cilia mechanically sense the direction of fluid flow for left-right determination. Science. 2023 Jan 6;379(6627):66-71. doi: 10.1126/science.abq8148. Epub 2023 Jan 5. PMID: 36603091.

Week #3 May 27
9:15-10:00 Joel Yisraeli (A. Fainsod)
Reading paper:
Lee H, Camuto CM, Niehrs C. R-Spondin 2 governs Xenopus left-right body axis formation by establishing an FGF signaling gradient. Nat Commun. 2024 Feb 2;15(1):1003. doi: 10.1038/s41467-024-44951-7.

10:15-12:00 Abraham Fainsod (J. Yisraeli)
Matthew-Wood Syndrome and retinoic acid signaling deficiency

Project paper:
Iturbide, A., Ruiz Tejeda Segura, M.L., Noll, C., Schorpp, K., Rothenaigner, I., Ruiz-Morales, E.R., Lubatti, G., Agami, A., Hadian, K., Scialdone, A., Torres-Padilla, M.-E., 2021. Retinoic acid signaling is critical during the totipotency window in early mammalian development. Nat. Struct. Mol. Biol. 28, 521□532. doi:10.1038/s41594-021-00590-w

Week #4 June 3
9:15-10:00 Abraham Fainsod (J. Yisraeli)
Reading paper:
Dickinson A.J.G., Turner S.D., Wahl S., Kennedy A.E., Wyatt B.H., Howton D.A. E-liquids and vanillin flavoring disrupts retinoic acid signaling and causes craniofacial defects in Xenopus embryos. Dev Biol. 2022 Jan;481:14-29. doi: 10.1016/j.ydbio.2021.09.004. Epub 2021 Sep 17. PMID: 34543654; PMCID: PMC8665092.

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Heart development and cardiomyopathies

Project paper:

Chen Y, L¼ttmann FF, Schoger E, Sch¶ler HR, Zelarayn LC, Kim KP, Haigh JJ, Kim J, Braun T. Reversible reprogramming of cardiomyocytes to a fetal state drives heart regeneration in mice. Science. 2021 Sep 24;373(6562):1537-1540. doi: 10.1126/science.abg5159. Epub 2021 Sep 23. PMID: 34554778.

Week #5 June 10
9:15-10:00 Joel Yisraeli (O. Gerlitz)
Reading paper:
Feng J, Li Y, Li Y, Yin Q, Li H, Li J, Zhou B, Meng J, Lian H, Wu M, Li Y, Dou K, Song W, Lu B, Liu L, Hu S, Nie Y. Versican Promotes Cardiomyocyte Proliferation and Cardiac Repair. Circulation. 2024 Mar 26;149(13):1004-1015. doi: 10.1161/CIRCULATIONAHA.123.066298. Epub 2023 Oct 27. PMID: 37886839.

10:15-12:00 Offer Gerlitz (J. Yisraeli)
Generation and interpretation of morphogen gradients (Tetra-amelia syndrome)

Project paper:
Xia ZJ, Zeng XI, Tambe M, Ng BG, Dong PDS, Freeze HH. A Dominant Heterozygous Mutation in COG4 Causes Saul-Wilson Syndrome, a Primordial Dwarfism, and Disrupts Zebrafish Development via Wnt Signaling. Front Cell Dev Biol. 2021 Sep 14;9:720688.

Week #6 June 17
9:15-10:00 Offer Gerlitz (J. Yisraeli)
Reading paper:
McGough IJ, Vecchia L, Bishop B, Malinauskas T, Beckett K, Joshi D, O'Reilly N, Siebold C, Jones EY, Vincent JP. Glypicans shield the Wnt lipid moiety to enable signalling at a distance Nature 2020 Sep;585(7823):85-90.

10:15-12:00 Joel Yisraeli (O. Gerlitz)
Planar Cell Polarity in Development and Disease

Project paper:
Takahashi-Kanemitsu A, Lu M, Knight CT, Yamamoto T, Hayashi T, Mii Y, Ooki T, Kikuchi I, Kikuchi A, Barker N, Susaki EA, Taira M, Hatakeyama M. The Helicobacter pylori CagA oncoprotein disrupts Wnt/PCP signaling and promotes hyperproliferation of pyloric gland base cells. Sci Signal. 2023 Jul 18;16(794):eabp9020. doi: 10.1126/scisignal.abp9020. Epub 2023 Jul 18. PMID: 37463245.

Week #7 June 24
9:15-10:00 Joel Yisraeli (A. Fainsod)
Reading paper:
Derrick CJ, Szenker-Ravi E, Santos-Ledo A, Alqahtani A, Yusof A, Eley L, Coleman AHL, Tohari S, Ng AY, Venkatesh B, Alharby E, Mansard L, Bonnet-Dupeyron MN, Roux AF, Vach© C, Roume J, Bouvagnet P, Almontashiri NAM, Henderson DJ, Reversade B, Chaudhry B. Functional analysis of germline VANGL2 variants using rescue assays of vangl2 knockout zebrafish. Hum Mol Genet. 2024 Jan 7;33(2):150-169. doi: 10.1093/hmg/ddad171. PMID: 37815931; PMCID: PMC10772043.

10:15-12:00 Abraham Fainsod (J. Yisraeli)
Pax3, Waardenburg Syndrome and muscle development

Project paper:
Esteves de Lima, J., Bou Akar, R., Mansour, M., Rocancourt, D., Buckingham, M., Relaix, F., 2021. M-Cadherin Is a PAX3 Target During Myotome Patterning. Front. Cell Dev. Biol. 9, 652652. doi:10.3389/fcell.2021.652652

Week #8 July 1
9:15-10:00 Abraham Fainsod (O. Gerlitz)
Reading paper:
Palmer, A.J., Savery, D., Massa, V., Copp, A.J., Greene, N.D.E., 2021. Genetic interaction of Pax3 mutation and canonical Wnt signaling modulates neural tube defects and neural crest abnormalities. Genesis 59, e23445. doi:10.1002/dvg.23445

10:15-12:00 Danny Ben-Zvi (A. Fainsod)
The developmental basis of obesity

Project paper:
Schellong, K., Melchior, K., Ziska, T., Henrich, W., Rancourt, R.C., Plagemann, A., 2020. Sex-specific epigenetic alterations of the hypothalamic Agrp-Pomc system do not explain □diabesity□ in the offspring of high-fat diet (HFD) overfed maternal rats. J. Nutr. Biochem. 75, 108257. doi:10.1016/j.jnutbio.2019.108257

Week #9 July 8
9:15-10:00 Danny Ben-Zvi (O. Gerlitz)
Reading paper:
Chang, G.-Q., Gaysinskaya, V., Karatayev, O., Leibowitz, S.F., 2008. Maternal high-

fat diet and fetal programming: increased proliferation of hypothalamic peptide-producing neurons that increase risk for overeating and obesity. J. Neurosci. 28, 12107–12119. doi:10.1523/JNEUROSCI.2642-08.2008

10:15-12:00 Offer Gerlitz (A. Fainsod)
Cell Competition in Development, Tissue Homeostasis (Aging) and Cancer

Project paper:
Ellis, S.J., Gomez, N.C., Levorse, J., Mertz, A.F., Ge, Y., Fuchs, E., 2019. Distinct modes of cell competition shape mammalian tissue morphogenesis. Nature 569, 497–502. doi:10.1038/s41586-019-1199-y

Week #10 July 15
9:15-10:00 Offer Gerlitz (A. Fainsod)

Reading paper:
Akieda Y, Ogamino S, Furuie H, Ishitani S, Akiyoshi R, Nogami J, Masuda T, Shimizu N, Ohkawa Y, Ishitani T., Cell competition corrects noisy Wnt morphogen gradients to achieve robust patterning in the zebrafish embryo. Nat Commun. 2019 Oct 17;10(1):4710. doi: 10.1038/s41467-019-12609-4

10:15-12:00 Abraham Fainsod (O. Gerlitz)
Scoliosis and the segmentation clock

Project paper:
Anderson, M.J., Magidson, V., Kageyama, R., Lewandoski, M., 2020. Fgf4 maintains Hes7 levels critical for normal somite segmentation clock function. eLife 9. doi:10.7554/eLife.55608

Week #11 July 22

9:15-10:00 Abraham Fainsod (O. Gerlitz)
Reading paper:
Matsuda, M., Hayashi, H., Garcia-Ojalvo, J., Yoshioka-Kobayashi, K., Kageyama, R., Yamanaka, Y., Ikeya, M., Toguchida, J., Alev, C., Ebisuya, M., 2020. Species-specific segmentation clock periods are due to differential biochemical reaction speeds.

Science 369, 1450–1455. doi:10.1126/science.aba7668

10:15-12:00 Ayal Ben-Zvi (A. Fainsod)
Blood vessels of the CNS - the angio-genesis vs barrier-genesis paradox

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Licht, T., Dor-Wollman, T., Ben-Zvi, A., Rothe, G., Keshet, E., 2015. Vessel maturation schedule determines vulnerability to neuronal injuries of prematurity. J. Clin. Invest. 125, 1319–1328. doi:10.1172/JCI79401
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<u>Required Reading:</u>
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Additional Reading Material:

Grading Scheme:
Presentation / Poster Presentation / Lecture/ Seminar / Pro-seminar / Research proposal 95 %
Active Participation / Team Assignment 5 %

Additional information: