



סילבוס

גנטיקה התפתחותית של מחלות באדם - 94921

תאריך עדכון אחרון 05-05-2024

נקודות זכות באוניברסיטה העברית: 3

היחידה האקדמית שאחראית על הקורס: מדעים ביורפואיים

השנה הראשונה בתואר בה ניתן ללמוד את הקורס: 0

סמסטר: סמסטר ב'

שפת ההוראה: אנגלית

קמפוס: עין כרם

מורה אחראי על הקורס (רכז): אברהם פיינסוד

דוא"ל של המורה האחראי על הקורס: abraham.fainsod@mail.huji.ac.il

שעות קבלה של רכז הקורס:

מורי הקורס:

פרופ אברהם פיינסוד,

פרופ עופר גרליץ,

פרופ יואל ישראלי,

פרופ איל בן-צבי,

פרופ דן בן-צבי

תאור כללי של הקורס:
הבסיס ההתפתחותי של מחלות האדם - נושאים נבחרים

מטרות הקורס:
להבין תהליכים בהתפתחות העובר היכולים להוביל למחלות גם בבוגר

תוצרי למידה
בסיומו של קורס זה, סטודנטים יהיו מסוגלים:
הבנה של תהליכים התפתחותיים בסיסיים

דרישות נוכחות (%) :
90

שיטת ההוראה בקורס: הרצאות וקראית מאמרים מודרכת

רשימת נושאים / תכנית הלימודים בקורס:

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 Tejada 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.*

10:15-12:00 Joel Yisraeli (A. Fainsod)

Heart development and cardiomyopathies

Project paper:

Chen Y, Lattmann FF, Schoger E, Schüller 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 VANG2 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 □diabetes□ 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

Project paper:

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

9:15-10:00 Ayal Ben-Zvi (A. Fainsod)

Reading paper:

Wang, Y., Rattner, A., Zhou, Y., Williams, J., Smallwood, P.M., Nathans, J., 2012. *Norrin/Frizzled4* signaling in retinal vascular development and blood brain barrier plasticity. *Cell* 151, 1332–1344. doi:10.1016/j.cell.2012.10.042

חומר חובה לקריאה:

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:

Kato 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 Tejada 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.

10:15-12:00 Joel Yisraeli (A. Fainsod)

Heart development and cardiomyopathies

Project paper:

Chen Y, Lattmann FF, Schoger E, Schaller 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 "diabetes" 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

Project paper:
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

9:15-10:00 Ayal Ben-Zvi (A. Fainsod)

Reading paper:
Wang, Y., Rattner, A., Zhou, Y., Williams, J., Smallwood, P.M., Nathans, J., 2012.

Norrin/Frizzled4 signaling in retinal vascular development and blood brain barrier plasticity. Cell 151, 1332–1344. doi:10.1016/j.cell.2012.10.042

חומר לקריאה נוספת:

מרכיבי הציון הסופי :
מצגת / הצגת פוסטר / הרצאה / סמינר / פרוסמינר / הצעת מחקר 95 %
השתתפות פעילה / עבודת צוות 5 %

מידע נוסף / הערות: