PPG-GENÉTICA E BIOLOGIA MOLECULAR
Disciplinas de Férias de Verão/2022

NI213 – IMUNOMETABOLISMO - TURMA PMV

Créditos: 6
Horário: Segundas-feiras a Quintas-feiras, das 9:00 às 13:00
Local/Sala: A DEFINIR
Período de oferecimento: Férias de Verão (de 10/01/2022 a 19/02/2022)
Vagas: 20
Mínimo de alunos: 10
Responsável: **Pedro Manoel Mendes de Moraes Vieira**
Estudantes especiais: Não aceita

PROGRAMA:
OBJETIVOS: Entender como o sistema imunológico pode modular e ser modulado por alterações metabólicas sistêmicas e celulares.
CONTEÚDO: Esta disciplina irá fornecer conceitos básicos e avançados de como o metabolismo influencia a resposta imune e como componentes imunológicos alteram o metabolismo sistêmico. O curso irá focar nos mecanismos moleculares que governam o metabolismo que fundamentam o funcionamento das células imunes, incluindo fosforilação oxidativa, metabolismo de aminoácidos, vias das pentoses, lipólise e lipogênese e glicólise. As vias metabólicas e imunológicas se cruzam em vários níveis e sua regulação é regulada por várias vias de sinalização hormonal que envolvem receptores específicos e adipocinas como PPARs, LXRs, leptina, grelina, adiponectina, RBP4, dentre outros que serão discutidos durante o curso. Finalmente, o conceito de imunometabolismo será aplicado a várias condições patológicas como em doenças autoimunes, obesidade e infecções.

Avaliação: Os alunos serão sorteados para definir quem irá apresentar o artigo no dia da apresentação.

CRONOGRAMA:
Avaliação: Os alunos serão sorteados para definir quem irá apresentar o artigo no dia da apresentação.
Em média, os alunos terão entre 3/4 artigos para lerem ao dia, para apresentarem no dia seguinte.
Obs.: Disciplina será ministrada ao longo de 3 semanas, com aulas diárias

Bloco 1
1. Newsholme, P., Curi, R., Gordon, S. & Newsholme, E. A. Metabolism of glucose, glutamine, long-chain fatty acids and ketone bodies by murine macrophages. Biochem. J. (1986).
2. Oren, R., Farnham, A. E., Saito, K., Milofsky, E. & Karnovsky, M. L. Metabolic patterns in three types of phagocytizing cells. J. Cell Biol. (1963).
3. West, A. P. et al. TLR signalling augments macrophage bactericidal activity through mitochondrial ROS. Nature (2011).

Bloco 2

1. Tannahill, G. M. et al. Succinate is an inflammatory signal that induces IL-1β through HIF-1α. Nature 496, 238–242 (2013).
2. Mills, E. L. et al. Succinate dehydrogenase supports metabolic repurposing of mitochondria to drive inflammatory macrophages. Cell 167, 457–470.e13 (2016).
3. Lampropoulou, V. et al. Itaconate links inhibition of succinate dehydrogenase with macrophage metabolic remodeling and regulation of inflammation. Cell Metab (2016).
4. Palsson-McDermott, E. M. et al. Pyruvate kinase M2 regulates Hif-1α activity and IL-1β induction and is a critical determinant of the warburg effect in LPS activated macrophages. Cell Metab. 21, 65–80 (2015)

Bloco 3

1. Jha, A. K. et al. Network integration of parallel metabolic and transcriptional data reveals metabolic modules that regulate macrophage polarization. Immunity (2015).
2. Gretchen Seim, et al. Two-stage metabolic remodelling in macrophages in response to lipopolysaccharide and interferon-γ stimulation. Nature Metabolism (2019).
3. Haschemi, A. et al. The sedoheptulose kinase CARKL directs macrophage polarization through control of glucose metabolism. Cell Metab. 15, 813–826 (2012).

Bloco 4

1. Pu-Ste Liu et al. α-ketoglutarate orchestrates macrophage activation through metabolic and epigenetic reprogramming. Nature Immunology (2017).
2. Puleston DJ et al. Polyamines and eIF5A Hypusination Modulate Mitochondrial Respiration and Macrophage Activation. Cell Metabolism (2019).
3. Garaude J et al. Mitochondrial respiratory-chain adaptations in macrophages contribute to antibacterial host defense. Nat. Immunology (2006).

Bloco 5

1. Bailey JD et al. Nitric Oxide Modulates Metabolic Remodeling in Inflammatory Macrophages through TCA Cycle Regulation and Itaconate Accumulation. Cell Reports (2019).
2. Cameron AM at al. Inflammatory macrophage dependence on NAD_+ salvage is a consequence of reactive oxygen species-mediated DNA damage. Nature Immunology (2019).
3. Divakaruni AS et al. Etomoxir Inhibits Macrophage Polarization by Disrupting CoA Homeostasis. Cell Metabolism (2018).

Bloco 6

1. Huang, S. C. et al. Cell-intrinsic lysosomal lipolysis is essential for alternative activation of macrophages. Nat. Immunol. 15, 846–855 (2014).
2. O'Neill, L. A. & Hardie, D. G. Metabolism of inflammation limited by AMPK and pseudo-starvation. Nature 493, 346–355 (2013).
3. Yumiko O et al. SREBP1 Contributes to Resolution of Proinflammatory TLR4 Signaling by Reprogramming Fatty Acid Metabolism. Cell Metabolism (2017).

Bloco 7

1. Donnelly, R. P. et al. mTORC1-dependent metabolic reprogramming is a prerequisite for NK cell effector function. J. Immunol. 193, 4477–4484 (2014).
2. Michalek, R. D. et al. Cutting edge: distinct glycolytic and lipid oxidative metabolic programs are essential for effector and regulatory CD4+ T cell subsets. J. Immunol (2011).
3. Krawczyk, C. M. et al. Toll-like receptor-induced changes in glycolytic metabolism regulate dendritic cell activation. Blood (2010).
4. Shi, L. Z. et al. HIF1α-dependent glycolytic pathway orchestrates a metabolic checkpoint for the differentiation of TH17 and Treg cells. J. Exp. Med (2011).

Bloco 8

1. Berod, L. et al. De novo fatty acid synthesis controls the fate between regulatory T and T helper 17 cells. Nat. Med. 20, 1327–1333 (2014).
2. Buck MD et al. Mitochondrial Dynamics Controls T Cell Fate through Metabolic Programming. Cell (2016).
3. Chang, C. H. et al. Posttranscriptional control of T cell effector function by aerobic glycolysis. Cell (2013).

Bloco 9

1. Delgoffe GM et al. The kinase mTOR regulates the differentiation of helper T cells through the selective activation of signaling by mTORC1 and mTORC2. Nat Immunol (2011).
2. Xu, T. et al. Metabolic control of TH17 and induced Treg cell balance by an epigenetic mechanism. Nature 548, 228–233 (2017).
3. Wang, R. et al. The transcription factor Myc controls metabolic reprogramming upon T lymphocyte activation. Immunity 35, 871–882 (2011).
4. Reis BS. Leptin receptor signaling in T cells is required for Th17 differentiation. Journal of Immunology (2015).

Bloco 10

3. Odegaard JI et. Al. Macrophage-specific PPARgamma controls alternative activation and improves insulin resistance. Nature (2007).
2. Wu D et al. Eosinophils sustain adipose alternatively activated macrophages associated with glucose homeostasis. Science (2011).
3. Silva HM et al. Vasculature-associated fat macrophages readily adapt to inflammatory and metabolic challenges. JEM (2019).

Bloco 11

1. Feuerer M et. Al. Lean, but not obese, fat is enriched for a unique population of regulatory T cells that affect metabolic parameters. Nature.
2. Vasanthakumar A. The transcriptional regulators IRF4, BATF and IL-33 orchestrate development and maintenance of adipose tissue-resident regulatory T cells. Nat Immunol. (2015).
3. Bapat SP et al. Depletion of fat-resident T_{reg} cells prevents age-associated insulin resistance. Nature (2015).

Bloco 12

1. Lee MW et. Al. Activated type 2 innate lymphoid cells regulate beige fat biogenesis. Cell (2015).
2. Cheng SC et al. mTOR- and HIF-1α-mediated aerobic glycolysis as metabolic basis for trained immunity. Science (2014).
3. Moraes-Vieira PM et al. RBP4 activates antigen-presenting cells, leading to adipose tissue inflammation and systemic insulin resistance. Cell Metabolism (2014).

BIBLIOGRAFIA:

Periódicos da área de estudo como: Science, nature, cell, nature immunology, cell metabolism, immunity, dentre outros.