



PLANO DE ENSINO AJUSTADO
SEMESTRE 2020 / 1

I. IDENTIFICAÇÃO DA DISCIPLINA: Mediadores da resposta Inflamatória

CÓDIGO	NOME DA DISCIPLINA	Alunos	CRÉDITOS	TOTAL DE HORAS-AULA SEMESTRAIS
PCM 3010	Mediadores da Resposta Inflamatória	Mestrado e Doutorado	03	45

I. HORÁRIO

SEXTAS-FEIRAS DAS 14:00 ÀS 18:00 HS

II. PROFESSOR (ES) MINISTRANTE (S)

Profª Drª. Tânia Silvia Fröde

III. EMENTA:

Entender a fisiopatologia da inflamação, conhecer os principais mediadores envolvidos na resposta inflamatória e correlacionar com várias doenças de caráter inflamatório.

IV. OBJETIVOS

Objetivos Gerais: Capacitar o acadêmico a conhecer e discutir sobre os principais mediadores envolvidos no processo inflamatório e em várias doenças de caráter inflamatório.

Objetivos Específicos:

- 1) Conhecer sobre a liberação e a expressão de mediadores inflamatórios por células envolvidas na resposta imune inata
- 2) Conhecer sobre os fatores de transcrição nuclear de células da resposta imune inata
- 3) Conhecer sobre os principais mecanismos envolvidos no apoptose celular
- 4) Conhecer sobre as principais vias de sinalização celular do tipo proteínas kinases (MAPK, JNK etc)
- 5) Conhecer o papel deste processo (mediadores inflamatórios, vias de sinalização, apoptose, fatores de transcrição nuclear) na fisiologia das doenças de caráter inflamatório agudo e crônico.
- 6) Conhecer sobre o mecanismo de ação anti-inflamatório de medicamentos atuais e daqueles em desenvolvimento no tratamento de doença de caráter inflamatório.

V. CONTEÚDO PROGRAMÁTICO

CONTEÚDO PROGRAMÁTICO	HORAS-AULA		ESTRATÉGIA
			Em virtude da pandemia do COVID-19 as atividades de ensino como ministrar seminários serão realizadas por webinar (plataforma Moodle-RNP)
1. liberação e expressão dos mediadores inflamatórios	03	03	Seminários
2. fatores de transcrição nuclear de células da resposta imune inata	03	03	Seminários
3. apoptose celular	03	03	Seminários
4. vias de sinalização celular	03	03	Seminários

5. doenças de caráter inflamatório agudo e crônico (apnéia, COVID-19, obesidade, câncer, Alzheimer etc...)	02	03	Seminários
6. Fármacos com propriedades anti-inflamatória: Dexametasona	01	03	Seminários

VI. METODOLOGIA DE ENSINO / DESENVOLVIMENTO DO PROGRAMA

Metodologia de ensino

Aulas Teóricas: exposição dialogada (já realizado)

Recursos utilizados: Web confêrencia via RNP (Moodle)

VII. METODOLOGIA DE AVALIAÇÃO

AVALIAÇÃO TEÓRICA

Serão realizadas dois (2) seminários por aluno. Cada aluna poderá escolher seus seminários da lista encaminhada a cada aluno.

AVALIAÇÃO POR SEMINÁRIO

Cada aluno irá apresentar dois seminários, distribuído pelo professor, via e-mail no primeiro dia de aula. Estes seminários também serão inseridos na plataforma Moodle-UFSC. Estes seminários **serão apresentados via webinar (plataforma Moodle-RNP) devido a pandemia do COVID-19. Nota final:** Avaliação da média dos seminários (dois para cada aluno). Nota mínima 7,0. Frequência 75%

VIII- Cronograma

DIA e horário	SEMINÁRIOS	DOCENTE - ALUNO
29.10 14:00- 18:00 h	Aula mediadores da resposta inflamatória	Tânia Silvia Frôde
5.11 14:00- 18:00 h	Aula mediadores da resposta inflamatória	Tânia Silvia Frôde
CRONOGRAMA		
12.11 14:00 - 15:00h	Immunopathology of Hyperinflammation in COVID-19. Gustine and Jones, 2021	
12.11 15:00- 16:00h	Pathological inflammation in patients with COVID-19: a key role for monocytes and macrophages. Merad and Martin, 2020	
12.11 16:00- 17:00h	Cytokine Storm in COVID-19: The Current Evidence and Treatment Strategies Tang et al., 2020	
12.11 17:00- 18:00h	Pulmonary Vascular Endothelialitis, Thrombosis, and Angiogenesis in Covid-19. Ackermann et al., 2020	
19.11 14:00 - 15:00h	Obstructive Sleep Apnea and Inflammation: Proof of Concept Based on Two Illustrative Cytokines. Kheirandish et al., 2019	
19.11 15:00- 16:00h	Neuropathological Features of Covid-19. 2021	
19.11 16:00- 17:00h	Dexamethasone in Hospitalized Patients with Covid-19, 2021	
19.11 17:00-	The Influence of Inflammation on Anemia in CKD Patients. Gluba-Brzózka et al., 2020	

18:00h		
26.11 14:00 - 15:00h	Inflammation and câncer. Murata, 2018	
26.11 15:00- 16:00h	Role of the NLRP3 Inflammasome: Insights Into Cancer Hallmarks. Lin et al., 2021	
26.11 16:00- 17:00h	Pathogenic role of exosomes and microRNAs in HPV-mediated inflammation and cervical cancer: A review. Nahand et al., 2019	
03.12 14:00 - 15:00h	Immunotherapy, Inflammation and Colorectal Cancer. Lichtenstern et al., 2020	
03.12 15:00- 16:00h	Endothelial Dysfunction in Obesity-Induced Inflammation: Molecular Mechanisms and Clinical Implications. Kwaifa et al., 2020	
03.12 16:00- 17:00h	Markers of inflammation and their association with muscle strength and mass: A systematic review and meta-analysis. Tuttle et al., 2020	
03.12 17:00- 18:00h	Multisystem Inflammatory Syndrome in U.S. Children and Adolescents. Feldstein et al., 2020	
10.12 14:00 - 15:00h	Role of pro-inflammatory cytokines released from microglia in Alzheimer's disease. Wang et al., 2015	
10.12 15:00- 16:00h		
10.12 16:00- 17:00h		
10.12 17:00- 18:00h		

XIX- BIBLIOGRAFIA BÁSICA

ANTONIOLI, L.; BLANDIZZI, C.; PACHER, P.; HASKÓ, G. Immunity, inflammation and cancer: a leading role for adenosine. *Nature Reviews Cancer*, v.13, n. 12, p. 842-857, 2013.

ARTHUR, J. S.; LEY, S. C. Mitogen-activated protein kinases in innate immunity. *Nature Reviews Immunology*, v. 13, n. 9, p. 679-692, 2013.

ASHLEY, N.T.; WEIL, Z. M.; NELSON, R. J. Inflammation: mechanisms, costs, and natural variation. *Annual Review of Ecology, Evolution, and Systematics*, v. 43, p. 385-406, 2012.

AYROLDI, E.; CANNARILE, L.; MIGLIORATI, G.; NOCENTINI, G.; DELFINO, D. V.; RICCARDI, C. Mechanisms of the anti-inflammatory effects of glucocorticoids: genomic and nongenomic interference with MAPK signaling pathways. *FASEB Journal*, v. 26, n. 12, p. 4805-4820, 2012.

BATRA, S.; BALAMAYOORAN, G.; SAHOO, M. K. Nuclear Factor- κ B: a key regulator in health and disease of lungs. *Archivum Immunologiae et Therapiae Experimentalis*, v. 59, p. 335-351, 2011.

BRENNER, D.; BLASER, H.; MAK, T. W. Regulation of tumour necrosis factor signalling: live or let die. *Nature Reviews Immunology*, v. 15, n. 6, p. 362-74, 2015.

BORISH, L. C.; STEINKE, J. W. Cytokines and chemokines. *Journal of Allergy and Clinical Immunology*, v. 111, n. 2, p. S460-475, 2003.

CALZADO, M. A.; BACHER, S.; SCHMITZ, M. L. NF-kappa B inhibitors for the treatment of inflammatory diseases and cancer. *Current Medicinal Chemistry*, v. 14, n. 3, p. 367-76, 2007.

CHANG, S. H.; DONG, C. Signaling of interleukin-17 family cytokines in immunity and inflammation. *Cellular Signalling*, v. 23, n. 7, p. 1069-1075, 2011.

CHOVATIYA, R.; MEDZHITOV, R. Stress, inflammation, and defense of homeostasis. *Molecular Cell*, v. 54, n. 2, p. 281-288, 2014.

COMMINS, S. P.; BORISH, L.; STEINKE, J. W. Immunologic messenger molecules: Cytokines, interferons, and chemokines. *Journal of Allergy and Clinical Immunology*, v. 125, n. 2, p. S53-S72, 2010.

CRUZ-TOPETE, D.; CIDLOWSKI, J. A. One hormone two actions: proinflammatory effect of glucocorticoids. *Neuroimmunomodulation*, v. 22, p. 20-32, 2015.

DELPORTE, C.; VAN ANTWERPEN, P.; VANHAMME, L.; ROUMEGUÈRE, T.; BOUDJELTIA, K. Z. Low-Density Lipoprotein Modified by Myeloperoxidase in Inflammatory Pathways and Clinical Studies. *Mediators of Inflammation*, v.13, 2013.

DIAMANT, G.; DIKSTEIN, R. Transcriptional control by NF-kappa B: elongation in focus. *Biochimica et Biophysica Acta*, v. 1829, n. 9, p. 937-945, 2013.

DINARELLO, C. A. Historical insights into cytokines. *European Journal of Immunology*, v. 37, p. 534-545, 2007.

DITTRICH, A.; HESSENKEMPER, W.; SCHAPER, F. Systems biology of IL-6, IL-12 family cytokines. *Cytokine & Growth Factor Reviews*, v. 26, p. 595-602, 2015.

DONG, W.; LIU, Y.; PENG, J.; CHEN, L.; ZOU, T.; XIAO, H.; LIU, Z.; LI, W.; BU, Y.; QI, Y. The IRAK-1-BCL10-MALT1-TRAF6-TAK1 cascade mediates signaling to NF-kappa B from Toll-like receptor 4. *Journal of Biological Chemistry*, v. 281, n. 36, p. 26029-26040, 2006.

DORWARD, D. A.; LUCAS, C. D.; ROSSI, A. G.; HASLETT, C.; DHALIWAL, K. Imaging inflammation: Molecular strategies to visualize key components of the inflammatory cascade, from initiation to resolution. *Pharmacology & Therapeutics*, v. 135, p. 182-199, 2012.

FAJGEENBAUM, D. C., JUNE, C. H. Cytokines storm. *New England of Medicine*, v. 383, n. 23, p. 2255-2273, 2020.

FONTES, J. A.; ROSE, N. R.; ČIHÁKOVÁ, D. The varying faces of IL-6: From cardiac protection to cardiac failure. *Cytokine*, v. 74, p. 62-68, 2015.

FRANCESCHI, C., SANTORO, A., CAPRI, M. The complex relationship between immunosenescence and inflammaging: special issue of the new biomedical perspectives., v. 42, p. 517-520, 2020.

GASPARINI, C.; CELEGHINI, C.; MONASTA, L.; ZAULI, G. NF-kappa B pathways in hematological malignancies. *Cellular and Molecular Life Sciences*, v. 71, n. 11, p. 2083-2102, 2014.

- GRETEN, F. R., GRIVENNIKOV, S. I., Inflammation and cancer: triggers, mechanisms, and consequences, v. 51, p. 27-41, 2019.
- HAYDEN, M.; GHOSH, S. Regulation of NF- κ B by TNF family cytokines. *Seminars in Immunology*, v. 26, n. 3, p. 253–266, 2014.
- HEADLAND, S. E.; NORLING, L. V. The resolution of inflammation: Principles and a challenges. *Seminars in Immunology*, v. 27, p. 149-160, 2015.
- HOESEL, B.; SCHMID, J. A. The complexity of NF- κ B signaling in inflammation and cancer. *Molecular Cancer*, v. 12, n. 86, p. 1-15, 2013.
- HOU, C.; LIN, H.; CHANG, C.; HUANG, W.; LIN, M. Oxidative stress and pyrogenic fever pathogenesis. *European Journal of Pharmacology*, v. 667, p. 6-12, 2011.
- HUANG, M., CAI, S, SU, J. Te pathogenesis of sepsis and potential therapeutic target, v. 20, p. 1-31, 2019.
- IP, W. K.; WONG, C. K; LAM, C. W. K. Interleukin (IL)-4 and IL-13 up-regulate monocyte chemoattractant protein-1 expression in human bronchial epithelial cells: involvement of p38 mitogen-activated protein kinase, extracellular signal-regulated kinase 1/2 and Janus kinase-2 but not c-Jun NH2-terminal kinase 1/2 signalling pathways. *Clinical & Experimental Immunology*, v. 145, n.1, p. 162–172, 2006.
- IYENGAR, N. M., GUCALP, A., DANNENBERG, A. J., HUDIS, C. Obesity and cancer mechanism: tumor microenvironment and inflammation, v. 34, n. 10, p. 4270-4276, 2016.
- KANG, S.; TANAKA, T.; KISHIMOTO, T. Therapeutic uses of anti-interleukin-6 receptor antibody. *International Immunology*, v. 27, n. 1, p. 21-29, 2015.
- KATO, Y. Neutrophil myeloperoxidase and its substrates: formation of specific markers and reactive compounds during inflammation, *Journal of Clinical Biochemistry and Nutrition*, v. 58, p. 99-104, 2016.
- KING, E.M.; CHIVERS, J. E.; RIDER, C. F.; MINNICH, A.; GIEMBYCZ M. A.; NEWTON, R. Glucocorticoid repression of inflammatory gene expression shows differential responsiveness by transactivation- and transrepression-dependent mechanisms. *PLoS ONE*, v. 8, n. 1, e53936, 2013.
- KOLACZKOWSKA, E.; KUBES, P. Neutrophil recruitment and function in health and inflammation. *Nature Reviews Immunology*, v. 13, p. 159-175, 2013.
- KOLATTUKUDY, P. E.; NIU, J. Inflammation, ER Stress, Autophagy and MCP-1/CCR2 Pathway. *Circulation Research*, v. 110, n. 1, p. 174-189, 2012.
- KVIETYS, P.; GRANGER, D. N. Role of reactive oxygen and nitrogen species in the vascular responses to inflammation. *Free Radical Biology & Medicine*, v. 52, p. 556-592, 2012.
- KUMAR, S.; BOEHM, J.; LEE, J. C. p38 MAP kinases: key signalling molecules as therapeutic targets for inflammatory diseases. *Nature Reviews Drug Discovery*, v. 2, n. 9, p. 717-726, 2003.
- LAEV, S. S.; SALAKHUTDINOV, N. F. Anti-arthritic agents: progress and potential. *Bioorganic & Medicinal Chemistry*, v. 23, p. 3059–3080, 2015.
- LARKIN III, J.; AHMED, C. M.; WILSON, T. D.; JOHNSON, H. M. Regulation of interferon gamma signaling by suppressors of cytokine signaling and regulatory T cells. *Frontiers in Immunology*, v. 18, n. 4, p. 1-8, 2013.

- LAROCCA, N. E.; MORENO, D.; GARMENDIA, J. V.; DE SANCTIS, J. B. Inhibitors of phosphoinositol 3 kinase and NF κ B for the treatment of chronic obstructive pulmonary disease. *Recent Patents on Inflammation & Allergy Drug Discovery*, v. 5, p. 178-183, 2011.
- LAWRENCE, T. The nuclear factor NF-kappa B pathway in inflammation. *Cold Spring Harbor Perspectives in Biology*, v. 1, n. 6, p. a001651, 2009.
- LEE, M. R.; DOMINGUEZ, C. MAP kinase p38 inhibitors: clinical results and an intimate look at their interactions with p38 alpha protein. *Current Medicinal Chemistry*, v. 12, n. 25, p. 2979-2994, 2005.
- MAK, J. C. W. Pathogenesis of COPD. Part II. Oxidative-antioxidative imbalance. *The International Journal of Tuberculosis and Lung Disease*, v. 12, p. 368-374, 2008.
- MANTOVANI, A.; CASSATELLA, M. A.; COSTANTINI, C.; JAILLON, S. Neutrophils in the activation and regulation of innate and adaptive immunity. *Nature Reviews Immunology*, v. 11, n. 8, p. 519-531, 2011.
- MAO, K.; CHEN, S.; CHEN, M.; MA, Y.; WANG, Y.; HUANG, B.; HE, Z.; ZENG, Y.; HU, Y.; SUN, S.; LI, J.; WU, X.; WANG, X.; STROBER, W.; CHEN, C.; MENG, G.; SUN, B. Nitric oxide suppresses NLRP3 inflammasome activation and protects against LPS-induced septic shock. *Cell Research*, v. 23, p. 201-12, 2013.
- MCGETTIGAN, P.; HENRY, D. Cardiovascular risk with non-steroidal anti-inflammatory drugs: systematic review of population-based controlled observational studies. *PLoS Medicine*, v. 8, n. 9, p. e1001098, 2011.
- MEDZHITOV, R.; HORNG, T. Transcriptional control of the inflammatory response. *Nature Reviews Immunology*, v. 9, n. 10, p. 692-703, 2009.
- NAGY, G.; CLARK, J. M.; BUZAS, E. I.; GORMAN, C. L.; COPE, A. P. Nitric oxide, chronic inflammation and autoimmunity. *Immunology Letters*, v. 111, p. 1-5, 2007.
- NEWTON, K.; DIXIT, V. M. Signaling in innate immunity and inflammation. *Cold Spring Harbor Perspectives in Biology*, v. 4, p. a006049, 2012.
- OECKINGHAUS, A.; HAYDEN, M. S.; GHOSH, S. Crosstalk in NF-kappa B signaling pathways. *Nature Immunology*, v. 12, n. 8, p. 695-708, 2011.
- PAPAYANNOPOULOS, V.; ZYCHLINSKY, A. NETs: a new strategy for using old weapons. *Trends of Immunology*, v. 30, n. 11, p. 513-521, 2009.
- PAYNE, A. S.; FREISHTAT, R. J. Conserved steroid hormone homology converges on NF κ B to modulate inflammation in asthma. *Journal of Investigative Medicine*, v. 60, n. 1, p. 13-17, 2012.
- POBER, J. S.; SESSA, W. C. Evolving functions of endothelial cells in inflammation. *Nature Reviews Immunology*, v. 7, p. 803-815, 2007.
- PREDONZANI, A.; CALÌ, B.; AGNELLINI, A. H.; MOLON, B. Spotlights on immunological effects of reactive nitrogen species: When inflammation says nitric oxide. *World Journal of Experimental Medicine*, v. 5, n. 2, p. 64-76, 2015.
- QUAX, R. A.; MENENSCHIJN, L.; KOPER, J. W.; HAZES, J. M.; LAMBERTS, S. W. J.; van ROSSUM, E. F. C.; FEELDERS, R. A. Glucocorticoid sensitivity in health and disease. *Nature Reviews Endocrinology*, v. 9, n. 11, p. 670-686, 2013.
- RATH, T.; BILLMEIER, U.; WALDNER, M. J.; ATREYA, R.; NEURATH, M. F. From physiology to disease and targeted therapy: interleukin-6 in inflammation and inflammation-associated carcinogenesis. *Archives of Toxicology*, v. 89, p. 541-554, 2015.

REA, I. M., GIBSON, D. S., MCGILLIGAN, V. MCNERLAN, S. E., ALEXANDER, H. D., ROSS, O. Age and age-related diseases: role of inflammation triggers and cytokines. *Frontiers in Immunology*, v;9, p. 1-28, 2018.

SACCANI, S.; PANTANO, S.; NATOLI, G. p38-Dependent marking of inflammatory genes for increased NF-kappa B recruitment. *Nature Immunology*, v. 3, n. 1, p. 69-75, 2002.

SADIK, C. D.; KIM, N. D.; LUSTER A. D. Neutrophils cascading their way to inflammation. *Trends in Immunology*. v. 32, n. 10, p. 452-460, 2011.

SAKLATVALA, J. The p38 MAP kinase pathway as a therapeutic target in inflammatory disease. *Current Opinion in Pharmacology*, v. 4, n. 4, p. 372-377, 2004.

SALLES, A.; ROMANO, A.; FREUDENTHAL, R. Synaptic NF-kappa B pathway in neuronal plasticity and memory. *Journal of Physiology-Paris*, v. 108, p. 256-262, 2014.

SCHAPER, F.; ROSE-JOHN, S. Interleukin-6: biology, signaling and strategies of blockade. *Cytokine & Growth Factor Reviews*, v. 26, p. 475-487, 2015.

SCHMID-SCHÖBEIN, G. W. Analysis of Inflammation. *Annual Review of Biomedical Engineering*, v. 8, p. 93-151, 2006.

SEDDER, L. M.; MCDERMOTT, M. F. TNF and TNF-receptors: From mediators of cell death and inflammation to therapeutic giants - past, present and future. *Cytokine & Growth Factor Reviews*, v. 25, n. 4, p. 453-72, 2014.

SHADHU, K., XI, C. inflammation and pancreatic cancer: An updated review. *Saudi Journal of Gastroenterology*, v. 25, n. 1, p. 3-13, 2019.

SINGH, N., BABY, D., PUJARI, V. B. Inflammation and cancer. *Annals of African Medicine*, v. 18, n. 3, p. 121-126, 2019.

SOEHNLEIN, O.; LINDBOM, L. Phagocyte partnership during the onset and resolution of inflammation. *Nature Reviews Immunology*, v. 10, p. 427-439, 2010.

STEWART, L.; KATIAL, R. K. Exhaled Nitric Oxide. *Immunology and Allergy Clinics of North America*, v. 32, n. 3, p. 347-362, 2012.

TRIPATHI, P.; TRIPATHI, P.; KASHYAP, L.; SINGH, V. The role of nitric oxide in inflammatory reactions. *FEMS Immunology and Medical Microbiology*, v. 51, p. 443-452, 2007.

VANDEVYVER, S.; DEJAGER, L.; TUCKERMANN, J.; LIBERT, C. New insights into the anti-inflammatory mechanisms of glucocorticoids: an emerging role for glucocorticoid-receptor-mediated transactivation. *Endocrinology*, v 154, n. 3, p. 993-1007, 2013.

YOKOTA, T, WANG, Y. p38 MAP kinases in the heart. *Gene*, v. 575, n. 2, p. 369-376, 2016.

ZARUBIN, T.; HAN, J. Activation and signaling of the p38 MAP kinase pathway. *Cell Research*, v. 15, n. 1, p. 11-18, 2005.

Bibliografia complementar

Seminários

