Contents

Editorials

- 185 Heme oxygenase-1 and dendritic cells: what else?
 - P. Blancou and I. Anegon

Accumulating evidence indicates that heme oxygenase-1 expression in dendritic cells could be the key step for providing and immune suppression through Tregs in many diseases or discorders.

- ► SEE CORRESPONDING ARTICLE ON PAGE 193
- 189 Maintaining the balance—fishing for drugs to treat persistent neutrophilic inflammation.

C. Hall and P. Crosier

The use of zebrafish as a platform to acclerate the discovery of therapeutic drugs that promote the resolution of neutrophilic inflammation is discussed.

SEE CORRESPONDING ARTICLE ON PAGE 203

Frontline Science

■PIVOTAL ADVANCE

- 193 Heme oxygenase 1 expression by human CD4⁺ T cells is not sufficient for their development of immunoregulatory capacity.
 - M. Biburger, G. Theiner, M. Schädle, G. Schuler, and G. Tiegs HO-1 induction in human T cells inhibits their proliferation, HO-1 suppression in Tregs increases their proliferation, but neither treatment fundamentally changes their respective suppressive capacity.
 - SEE CORRESPONDING EDITORIAL ON PAGE 185
- 203 Pharmacological manipulation of inflammation resolution during spontaneously resolving tissue neutrophilia in the zebrafish.

C. A. Loynes, J. S. Martin, A. Robertson, D. M. I. Trushell,

P. W. Ingham, M. K. B. Whyte, and S. A. Renshaw

The resolution of neutrophilic inflammation in the zebrafish can be visualized in vivo and manipulated by a range of pharmacological mediators, demonstrating a role for neutrophil apoptosis in this process.

SEE CORRESPONDING EDITORIAL ON PAGE 189

■REVIEWS

- 213 Immunopathogenesis of polymicrobial otitis media.
 - L. O. Bakaletz

The synergistic relationship between URT viruses and bacteria in OM pathogenesis is not fully understood, but overall is predicated on viral impairment of airway defenses.

223 ■ HVEM/LIGHT/BTLA/CD160 cosignaling pathways as targets for immune regulation.

M. L. del Rio, C. L. Lucas, L. Buhler, G. Rayat, and J. I. Rodriguez-Barbosa

This review highlights how the blockade of the co-stimulatory HVEM/LIGHT interaction or agonist signaling through the inhibitory BTLA and CD160 receptors could contribute to the control of deleterious immune responses.

The battlefield of perforin/granzyme cell death pathways.

. Hoves, J. A. Trapani, and I. Voskoboinik

The review discusses the controversies in the field of cytotoxic lymphocyte secretory granule death pathways.

Research

Cell Development, Differentiation, & Trafficking

- 245 Biogenesis of secretory organelles during B cell differentiation.
 - S. J. Kirk, J. M. Cliff, J. A. Thomas, and T. H. Ward
 In differentiating B cells, proliferation of endoplasmic reticulum appears as tightly clustered juxtanuclear spherical structures which expand to fill the cytosol without synchronizing to cell expansion.
- 257 Ref. Antigen-induced Erk1/2 activation regulates Ets-1-mediated sensitization of CD8+ T cells for IL-12 responses.
 - Q. Li, C. Eppolito, K. Odunsi, and P. A. Shrikant The molecular basis of collaboration between instructions that program CD8+ T cells for long-term responses.
- 265 Induction of HIF- 1α and the glycolytic pathway alters apoptotic and differentiation profiles of activated human T cells.
 - A. Larbi, H. Zelba, D. Goldeck, and G. Pawelec
 T cell differentiation and functions are altered at low oxygen, possibly via HIF-1α and glycolysis up-regulation.

Receptors, Signal Transduction, & Genes

- 275 Phagosomal retention of Francisella tularensis results in TIRAP/Mal-independent TLR2 signaling.
 - L. E. Cole, M. H. W. Laird, A. Seekatz, A. Santiago, Z. Jiang, E. Barry, K. A. Shirey, K. A. Fitzgerald, and S. N. Vogel

Enhanced or prolonged interaction between an agonist and TLR2 can overcome the need for TIRAP.

KEY: BCR Brief Conclusive Report



283 Mesenchymal stem cells respond to TNF but do not produce TNF.

L. C. J. van den Berk, B. J. H. Jansen, K. G. C. Siebers-Vermeulen, H. Roelofs, C. G. Figdor, G. J. Adema, and R. Torensma

The TNF promoter is silenced in mesenchymal stem cells able to respond to LPS by NFkB translocation and cytokine production yet without TNF.

291 Syk expression in peripheral blood leukocytes, CD34+ progenitors, and CD34-derived basophils.

S. S. Ishmael and D. W. MacGlashan Jr.

The critical signaling kinase of IgE-mediated reactions, syk, can be down-regulated in maturing basophils by chronic aggregation without altering their expression of FceRI, granule staining, and histamine content.

Inflammation, Extracellular Mediators, & Effector Molecules

- 301 ICOS promotes IL-17 synthesis in colonic intraepithelial lymphocytes in IL-10^{-/-} mice.
 - J. S. Schaefer, D. Montufar-Solis, N. Vigneswaran, and J. R. Klein IL-23 and IL-10 have opposing effects on IL-17 synthesis by mouse ICOS⁺ T cells in the colonic epithelium.
- 309 Liver X receptor agonist treatment reduced splanchnic ischemia and reperfusion injury.

C. Crisafulli, R. Di Paola, E. Mazzon, I. Paterniti, M. Galuppo,

T. Genovese, P. Bramanti, A. Cappellañi, and S. Cuzzocrea
T0901317, LXR receptor agonist, reduces the inflammatory
response and the ileum injury associated to splanchnic artery
occlusion shock.

323 Leukotriene B₄ mediates γδ T lymphocyte migration in response to diverse stimuli.

M. F. de Souza Costa, R. de Souza-Martins, M. C. de Souza, C. F. Benjamim, B. Piva, B. L. Diaz, M. Peters-Golden, M. das Graças Henriques, C. Canetti, and C. Penido

 $\gamma\delta$ T cell migration into mouse pleural cavities during inflammatory responses triggered by LPS, *Mycobacterium bovis* BCG, or ovalbumin depends on leukotriene B₄ and BLT1 receptor.

Host Defense & Pathophysiology

333 Regulation of macrophage motility by Irgm1.

S. C. Henry, M. Traver, X. Daniell, M. Indaram, T. Oliver, and G. A. Taylor

Irgm1 controls macrophage motility by regulating the positioning of specific GKS IRG proteins to the plasma membrane, leading to altered Rac activity and actin remodelling.

Translational & Clinical Immunology

- 345 Adenosine A_{2A} receptor activation limits graftversus-host disease after allogenic hematopoietic stem cell transplantation.
 - C. M. Lappas, P.-C. Liu, J. Linden, E. M. Kang, and H. L. Malech The selective activation of the A_{2A} has therapeutic potential in both the prevention and treatment of acute GVHD.

ON THE COVER:



Lack of Irgm1 localization at the leading edge of motile macrophages—see Henry et al., "Regulation of macrophage motility by Irgm1," page 333.