

CANCER IMMUNOLOGY RESEARCH

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Olivier Lantz
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- 997 **Q&A: Lisa H. Butterfield, Elizabeth M. Jaffee, and Arlene H. Sharpe on the SITC-AACR Joint Workshop, "The Cancer Biology Underlying Immunotherapy-Induced Autoimmunity"**

PRIORITY BRIEF

- 999 **CRASH-IT Switch Enables Reversible and Dose-Dependent Control of TCR and CAR T-cell Function**
Ali Can Sahillioglu, Mireille Toebe, Georgi Apriamashvili, Raquel Gomez, and Ton N. Schumacher
The authors report a modular T-cell control system, CRASH-IT, that allows the function of T cells activated by their TCR or genetically introduced TCRs or CARs to be adjusted in a reversible manner over a wide dynamic range.

RESEARCH ARTICLES

- 1008 **Overproduction of Gastrointestinal 5-HT Promotes Colitis-Associated Colorectal Cancer Progression via Enhancing NLRP3 Inflammasome Activation**
Tao Li, Bin Fu, Xin Zhang, Yunjiang Zhou, Mengdi Yang, Mengran Cao, Yaxin Chen, Yingying Tan, and Rong Hu
A 5-HT-NLRP3 positive feedback loop is demonstrated to maintain persistent inflammation in the colon, resulting in promotion of CRC development and progression. The data highlight the potential to target this feedback loop as a CRC therapeutic strategy.

- 1024 **Activating Mucosal-Associated Invariant T Cells Induces a Broad Antitumor Response**

Benjamin Ruf, Vanessa V. Catania, Simon Wabitsch, Chi Ma, Laurence P. Diggs, Qianfei Zhang, Bernd Heinrich, Varun Subramanyam, Linda L. Cui, Marie Pouzolles, Christine N. Evans, Raj Chari, Shunsuke Sakai, Sangmi Oh, Clifton E. Barry III, Daniel L. Barber, and Tim F. Greten

In vitro evidence suggests mucosal-associated invariant T (MAIT) cells can have antitumor function. This study shows MAIT cells stimulated *in vivo* using 5-OP-RU and CpG orchestrate potent antitumor responses, suggesting these cells as potential targets for cancer immunotherapy.

See related Spotlight, p. 996

- 1035 **Development of a Clinically Relevant Reporter for Chimeric Antigen Receptor T-cell Expansion, Trafficking, and Toxicity**

Reona Sakemura, Aditya Bansal, Elizabeth L. Siegler, Mehrdad Hefazi, Nan Yang, Roman H. Khadka, Alysha N. Newsom, Michael J. Hansen, Michelle J. Cox, Claudia Manriquez Roman, Kendall J. Schick, Ismail Can, Erin E. Tapper, Wendy K. Nevala, Mohamad M. Adada, Evandro D. Bezerra, Lionel Aurelien Kankeu Fonkoua, Paulina Horvei, Michael W. Ruff, Sameer A. Parikh, Mukesh K. Pandey, Timothy R. DeGrado, Lukkana Suksanpaisan, Neil E. Kay, Kah-Whye Peng, Stephen J. Russell, and Saad S. Kenderian

Currently, a robust imaging platform to monitor CART cells is lacking. Imaging using 18F-TFB-PET is demonstrated to be an efficient, noninvasive technique to monitor CART-cell expansion and trafficking *in vivo* in multiple tumor models.

- 1047 **Rationally Designed Transgene-Encoded Cell-Surface Polypeptide Tag for Multiplexed Programming of CAR T-cell Synthetic Outputs**

Adam J. Johnson, Jia Wei, James M. Rosser, Annette Künkele, Cindy A. Chang, Aquene N. Reid, and Michael C. Jensen

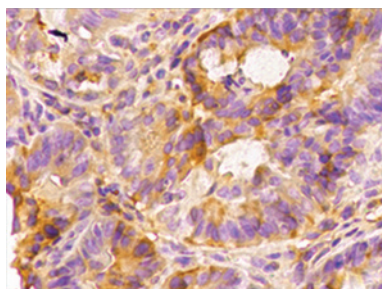
The authors describe a cell-surface tag system that allows the generation of CAR T cells that recognize more than one target or carry the complex synthetic biology payloads needed to overcome current challenges to advancing CAR T-cell therapy.

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- 1061 CD19/CD22 Dual-Targeted CAR T-cell Therapy for Relapsed/Refractory Aggressive B-cell Lymphoma: A Safety and Efficacy Study**
Guoqing Wei, Yanlei Zhang, Houli Zhao, Yiyun Wang, Yandan Liu, Bin Liang, Xiujian Wang, Huijun Xu, Jiazhen Cui, Wenjun Wu, Kui Zhao, Arnon Nagler, Alex H. Chang, Yongxian Hu, and He Huang
This clinical trial shows CD19/CD22 dual-targeted CAR T cells yield potent and durable responses for patients with B-cell lymphoma without severe cytokine release syndrome, suggesting a way to overcome the antigen-negative relapse seen with monospecific CAR T cells.
- 1071 A Fusion Protein Complex that Combines IL-12, IL-15, and IL-18 Signaling to Induce Memory-Like NK Cells for Cancer Immunotherapy**
Michelle K. Becker-Hapak, Niraj Shrestha, Ethan McClain, Michael J. Dee, Pallavi Chaturvedi, Gilles M. Leclerc, Lynne I. Marsala, Mark Foster, Timothy Schappe, Jennifer Tran, Sweta Desai, Carly C. Neal, Patrick Pence, Pamela Wong, Julia A. Wagner, David A. Russler-Germain, Xiaoyun Zhu, Catherine M. Spanoudis, Victor L. Gallo, Christian A. Echeverri, Laritza L. Ramirez, Lijing You, Jack O. Egan, Peter R. Rhode, Jin-an Jiao, Gabriela J. Muniz, Emily K. Jeng, Caitlin A. Prendes, Ryan P. Sullivan, Melissa M. Berrien-Elliott, Hing C. Wong, and Todd A. Fehniger
A scalable platform, with GMP application, that can be used to generate a multitude of different heteromeric proteins is presented. The platform's use to generate memory-like NK cells for immunotherapy is demonstrated and provides insights into their biology.
- 1088 TIGIT-Fc Promotes Antitumor Immunity**
Xian Shen, Wenyan Fu, Yongpeng Wei, Junle Zhu, Yue Yu, Changhai Lei, Jian Zhao, and Shi Hu
A TIGIT-Fc fusion protein is demonstrated to modulate NK-cell and T-cell antitumor responses. Treatment leads to generation of immune memory and enhances efficacy of immune checkpoint blockade, highlighting its promise as a cancer immunotherapy.
- 1098 CD86⁺ Antigen-Presenting B Cells Are Increased in Cancer, Localize in Tertiary Lymphoid Structures, and Induce Specific T-cell Responses**
Kerstin Wennhold, Martin Thelen, Jonas Lehmann, Simon Schran, Ella Preugszat, Maria Garcia-Marquez, Axel Lechner, Alexander Shimabukuro-Vornhagen, Meryem S. Ercanoglu, Florian Klein, Fabinsky Thangarajah, Sebastian Eidt, Heike Löser, Christiane Bruns, Alexander Quaas, Michael von Bergwelt-Baildon, and Hans A. Schlößer
B cells are shown to be present in multiple cancer types and could be potential immunotherapeutic targets. These cells localize to tertiary lymphoid structures in the tumor microenvironment and through antigen presentation induce antigen-specific T-cell responses.

ABOUT THE COVER

The neurotransmitter 5-hydroxytryptamine (5-HT) promotes gastrointestinal inflammation, a process that can facilitate development of colitis-associated cancer. Li and Fu et al. find that the rate-limiting enzyme in 5-HT synthesis is upregulated in tumor tissues of mouse models, as well as patients with colorectal cancer. Tumor cell-derived 5-HT leads to inflammasome activation in macrophages via HTR3A (5-hydroxytryptamine receptor 3A), an ion channel receptor, and the resulting calcium influx. Interestingly, inflammasome-mediated IL1 β release from macrophages then further promotes tumor cell 5-HT production, demonstrating a positive feedback loop that has potential to be therapeutically targeted. Read more in this issue on page 1008. Original image from Fig. 7I. Artwork by Lewis Long.



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