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EurekAlert

EDITOR'S PICK: Alpha-2 integrin: a protein predictor of tumor spread?

Mary Zutter and colleagues, at Vanderbilt University Medical Center, Nashville, have generated data that lead them to suggest that decreased expression of the protein alpha-2 integrin is predictive of tumor dissemination to distant sites and decreased survival in individuals with either breast or prostate cancer.

The researchers first studied the role of the protein alpha-2-beta-1 integrin (which is composed of the alpha-2 integrin protein and the beta-1 integrin protein) in cancer initiation and progression using a clinically relevant, spontaneous mouse model of breast cancer progression and metastasis (spread). Their data indicated that alpha-2-beta-1 integrin suppressed metastasis. To investigate whether the data had any immediate clinical applicability, a systematic analysis of microarray databases of human breast and prostate cancer was performed. The results of this analysis showed that decreased expression of the gene responsible for generating alpha-2 integrin was predictive of metastasis and decreased survival, leading to the suggestion that alpha-2 integrin expression could be a useful biomarker of metastatic potential and patient survival.

TITLE: The alpha-2-beta-1 integrin is a metastasis suppressor in mouse models and human cancer

AUTHOR CONTACT:
Mary M. Zutter
Vanderbilt University Medical Center, Nashville, Tennessee, USA.
Phone: 615.343.1095; Fax: 615.343.7040; E-mail: mary.zutter@vanderbilt.edu [1].

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EDITOR'S PICK: A DEDD cert to support embryo development

The mammalian embryo relies on physical connections to its mother to survive. After implantation into the wall of the uterus and before the placenta is established, a structure known as the decidua forms and is key to supporting embryonic development. Defective formation of an effective decidua is thought to be a cause of female infertility. A team of researchers, led by Toru Miyazaki, at the University of Tokyo, Japan, has now determined that the protein DEDD is required for the formation of a functional decidua in mice. The authors therefore suggest that it would be interesting to investigate whether DEDD dysfunction is the cause of infertility in some women.

TITLE: Death effector domaincontaining protein (DEDD) is required for uterine decidualization during early pregnancy in mice

AUTHOR CONTACT:
Toru Miyazaki
Center for Disease Biology and Integrative Medicine, The University of Tokyo, Tokyo, Japan.
Phone: 81.3.5841.1435; Fax: 81.3.5841.1438; E-mail: tm@m.u-tokyo.ac.jp [3].

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EDITOR'S PICK: How bacteria get from catheter to patient

Patients in hospitals and healthcare facilities can develop infections as a result of contamination of indwelling medical devices such as catheters with bacteria that are normal inhabitants of the skin of the patient or health care personnel. The bacterium *Staphylococcus epidermidis* is a major cause of such infections. This is in part because of its ability to form biofilms — surface-attached agglomerations of microorganisms that are extremely difficult to eradicate — on indwelling devices. Michael Otto and colleagues, at the National Institutes of Health, Bethesda, have now identified the bacterial products that enable *Staphylococcus epidermidis* biofilms to detach from the surface to which they are adhered and cause infection in a mouse model of catheterization. Importantly, molecules known as antibodies that target these bacterial products inhibited bacterial spread in the mouse model, leading the authors to suggest that interfering with biofilm detachment mechanisms might provide a new approach to preventing biofilm-associated infections.

TITLE: *Staphylococcus epidermidis* surfactant peptides promote biofilm maturation and dissemination of biofilm-associated infection in mice

AUTHOR CONTACT:
Michael Otto
National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland, USA.
Phone: 301.443.5209; Fax: 301.480.3633; E-mail: motto@niaid.nih.gov [5].

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DERMATOLOGY: Targeting blood vessel growth to treat psoriasis

Psoriasis is a common skin disorder that arises when immune cells become overactive and generate unneeded inflammatory responses in the skin.

Dysregulated growth of new blood vessels from pre-existing vessels (a process known as angiogenesis) is one hallmark of psoriasis, which is also characterized by thick silvery scales on affected areas of skin and itchy, dry, red patches. A team of researchers, led by Michael Schön, at Georg August University, Germany, has now found that reducing angiogenesis in xenotransplantation models of psoriasis and in mice with a disease that resembles psoriasis alleviates disease. They therefore suggest that their non-viral gene therapy approach to reducing angiogenesis might provide a new approach to treating psoriasis and, perhaps, other inflammatory skin disorders characterized by dysregulated angiogenesis.

TITLE: Halting angiogenesis by non-viral somatic gene therapy alleviates psoriasis and murine psoriasiform skin lesions

AUTHOR CONTACT:
Michael P. Schön
Georg August University, Göttingen, Germany.
Phone: 49.551.39.6401; Fax: 49.551.39.6841;
E-mail: michael.schoen@med.uni-goettingen.de [7].

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VIROLOGY: How hepatitis C virus uses the cells it infects to its own advantage

The current therapy to treat individuals infected with hepatitis C virus (HCV) works in only about half of those treated. Therefore, many individuals remain chronically infected with HCV, something that often leads to liver failure and liver cancer. Research using human liver cell lines, performed by Po-Yuan Ke and Steve Chen, at Academia Sinica, Taiwan, has identified new ways in which HCV coopts normal cellular processes in the cells that it infects to enhance its reproduction and to evade certain aspects of the antiviral immune response. These data not only provide new insight into the ways in which interactions between HCV and the cells it infects can benefit the virus, but also provide potential new avenues of research for the development of novel therapeutic approaches to clearing HCV infection.

TITLE: Activation of the unfolded protein response and autophagy after hepatitis C virus infection suppresses innate antiviral immunity in vitro

AUTHOR CONTACT:
Steve S.-L. Chen
Institute of Biomedical Sciences, Academia Sinica, Taipei, Taiwan.
Phone: 886.2.2652.3933; Fax: 886.2.2652.3073; E-mail: schen@ibms.sinica.edu.tw [9].

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http://www.jci.org/articles/view/41474?key=b8efc145f04abae00e4e [10]

PULMONARY: Pinpointing a role for the molecule TGF-beta in lung scarring

Idiopathic pulmonary fibrosis (IPF) is a chronic lung disorder for which there are currently no treatments. It is a progressive disease that results in lung scarring and changes in lung architecture, which together lead to loss of lung function and death. Although the cause(s) of IPF is unclear, dysregulated signaling triggered by the molecule TGF-beta is known to have a role in disease development. Parviz Minoo, Zea Borok, and colleagues, at the University of Southern California, Los Angeles, have now been able to more specifically pinpoint the role of dysregulated TGF-beta signaling in disease development using a mouse model of lung fibrosis (scarring).

The researchers generated mice lacking T-beta-RII — the molecule to which TGF-beta binds to trigger a signaling cascade — on cells lining the lung (epithelial cells). Importantly, these mice showed increased survival and resistance to fibrosis in the chemical-induced model of fibrosis studied. The authors therefore suggest that T-beta-RII could provide a new target for the development of therapeutics to treat IPF.

TITLE: Epithelium-specific deletion of TGF-beta receptor type II protects mice from bleomycin-induced pulmonary fibrosis

AUTHOR CONTACT:
Parviz Minoo
University of Southern California, Los Angeles, California, USA.
Phone: 323.226.4340; Fax: 213.236.5049; E-mail: minoo@usc.edu [11].

Zea Borok
Keck School of Medicine of the University of Southern California, Los Angeles, California, USA.
Phone: 323.226.7923; Fax: 323.226.2738; E-mail: zborok@usc.edu [12].

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MUSCLE BIOLOGY: Linking two previously disparate muscle diseases

Individuals with mutations in their DES gene have dysfunctional muscle fibers in their skeletal and heart muscle (conditions termed myopathy and cardiomyopathy, respectively). This leads to progressive skeletal muscle weakness and heart failure. A team of researchers, led by Jocelyn Laporte, at the Institut de Génétique et de Biologie Moléculaire et Cellulaire, France, has now determined that the mechanisms underlying disease in individuals with a previously unrelated form of inherited myopathy (X-linked centronuclear myopathy [XLCNM]) are similar to those in individuals with DES gene mutations. Specifically, they found that the protein generated by the gene mutated in individuals with XLCNM (MTM1) binds desmin

(the product of the DES gene) and ensures normal desmin expression and localization in both both mouse and human skeletal muscles. These and other data in the paper lead the authors to suggest that XLCNM and desmin-related myopathy, two conditions thought previously to be unrelated, have common disease-related features.

TITLE: Myotubularin controls desmin intermediate filament architecture and mitochondrial dynamics in human and mouse skeletal muscle

AUTHOR CONTACT:
Jocelyn Laporte
Institut de Génétique et de Biologie Moléculaire et Cellulaire, Illkirch, France.
Phone: 33.388653412; Fax: 33.388653201; E-mail: mtm@igbmc.fr [14].

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OPHTHALMOLOGY: Support for light-sensing cells eroded by the mTOR signaling pathway

The retina is the light-sensitive tissue that lines the inner surface of the eye. It consists of light-sensitive nerve cells known as photoreceptors and cells that support and nourish the photoreceptors, which are known as retinal pigment epithelial (RPE) cells. RPE cell dysfunction leads to retinal degeneration and loss of visual acuity. A team of researchers, led by Douglas Vollrath, at Stanford University School of Medicine, Stanford, has now determined in mice that stresses that disrupt the function of the energy generating compartments within RPE cells (mitochondria) trigger RPE cell dedifferentiation and that this leads to decreased responsiveness of photoreceptor cells to light and their eventual degeneration. Further analysis revealed that RPE cell dedifferentiation involved the signaling protein mTOR and that the mTOR inhibitor rapamycin protected photoreceptor function in response to RPE stresses. The authors therefore suggest that mTOR pathway inhibitors might provide a new approach to treating individuals with retinal degenerative diseases involving RPE stress.

TITLE: mTOR-mediated dedifferentiation of the retinal pigment epithelium initiates photoreceptor degeneration in mice

AUTHOR CONTACT:
Douglas Vollrath
Stanford University School of Medicine, Stanford, California, USA.
Phone: 650.723.3290; Fax: 650.723.7016; E-mail: vollrath@stanford.edu [16].

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IMMUNOLOGY: Understanding how single immune cells "see" their target

Key to designing effective vaccines and immune-based therapeutics for the treatment of autoimmune diseases such as rheumatoid arthritis is characterizing in detail the immune cells (T cells) that naturally respond to the microbe or cause the autoimmune disease. One facet of this characterization is to define very specifically the protein complex expressed by T cells (the T cell receptor [TCR]) that enables them to "see" their target and respond to microbes or cause autoimmunity. A team of researchers, led by Paul Thomas, at St Jude Children's Research Hospital, Memphis, has now developed a new method to examine the TCR expressed by an individual T cell, an approach that they hope will prove of tremendous use for researchers studying mouse models of human disease.

TITLE: Paired analysis of TCR-alpha and TCR-beta chains at the single-cell level in mice

AUTHOR CONTACT:
Paul G. Thomas
St Jude Children's Research Hospital, Memphis, Tennessee, USA.
Phone: 901.595.6507; Fax: 901.595.3107; E-mail: paul.thomas@stjude.org [18].

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