From: F1000 Biology Update <[redacted]>
To: Jeff Epstein <jeeproject@yahoo.com>
Subject: Disease-mediated trophic cascades in the Serengeti and how to inhibit the mycobacterial proteasome.
Date: Wed, 18 Nov 2009 16:27:17 +0000

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Richard Grant explains the role of Associate Faculty Members on our blog and more videos from our visit to the Society for Neuroscience meeting in Chicago have been posted on our Youtube channel.

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Editor's Choice: A disease-mediated trophic cascade in the Serengeti and its implications for ecosystem C

Few global issues receive as much attention as the carbon cycle and climate change, and for good reason. Trees are known to be a major carbon sink and, as such, rainforests have been the focus of increased protection. However, a recent study published in PLoS Biology, highlighted by Blake Suttle and Oswald Schmitz of the Ecology Faculty, has shown that disease control in herbivores in the Serengeti had the surprising effect of creating a new carbon sink out of a previous net carbon source.

Blake Suttle and Oswald Schmitz explain

> "This exceptional study addresses the applied question of what regulates tree cover in African savannas while also building basic ecological theory on disease as a top-down driver of ecosystem dynamics."

They continue

> "Bayesian state-space models reveal that eradication of rinderpest virus in the 1960s led to an irruption in the Serengeti wildebeest population, which increased grazing pressure on savanna grasses and decreased fuel loads, in turn, reducing fire frequency, the primary direct determinant of savanna tree density over large spatial scales."

And conclude

> "In a fascinating twist, [the authors] close with an exploration of the modern management implications of their work, suggesting that local governments could draw revenues for carbon sequestration based on maintaining a large grazer herd, selling carbon offsets to visitors and the emerging international market."

Read all comments in full.

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Broad Impact: Inhibiting the mycobacterial proteasome

In this must-read article, the authors found that some oxathiazol-2-one compounds can kill non-replicating Mycobacterium tuberculosis by inhibiting the proteasome. As tuberculosis is a major global health problem, this research is potentially very important.

Adam S Duerfeldt and Brian Blagg of the Pharmacology & Drug Discovery Faculty explain

> "Tuberculosis is a contagious and deadly disease that infects roughly one third of the world's population. The current treatment regimen was developed in the 1970s and involves a minimum 6-month treatment with drug cocktails."

Jean Pieters of the Microbiology Faculty continues

> "During latent mycobacterial infection, non-replicative status causes longer treatment of disease with conventional anti-mycobacteria agents than any other infectious disease, possibly leading to the emergence of drug-resistant strains or failure of therapy."

Karin Romisch of the Cell Biology Faculty goes on to say

"Despite structural differences, most known proteasome inhibitors affect both human and mycobacterial proteasomes and therefore cannot be used as treatment for tuberculosis. The authors of this paper screened a drug library and found two new compounds which specifically inhibit the mycobacterial proteasome."

However, Bradley Morgan of the Pharmacology & Drug Discovery Faculty warns

"The oxathiazol-2-one compounds discovered in the paper are not likely to result in useful drug candidates due to the relative instability of this moiety in a biological milieu, as represented by the half-life of the analogs in RPMI medium, which is shown in the supplemental material. Nevertheless, this paper demonstrates the possibility of identifying and designing specific inhibitors of the proteasomes of pathogenic organisms that are becoming resistant to current therapies."

Read all comments in full.

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Hidden Jewel: Extracellular DNA is required for root tip resistance to fungal infection

This paper, selected by Tal Isaacson and Jocelyn Rose of the Plant Biology Faculty, describes how root cap cells in peas secrete DNA to defend against fungal pathogens.

Tal Isascson and Jocelyn Rose explain

"It has been known for some time that the tips of roots are far more resistant to infection by microbial pathogens than the adjacent elongation zone, and there are good reasons for

thinking that the secreted mucilage from the root caps contributes to this phenomenon."

They continue

"...depolymerizing the DNA results in enhanced infection by the fungus Nectria haematococca and …the rate of that depolymerization shows some correspondence to the rate of infection. Radiolabeling is used to show that the secreted DNA is synthesized by living cells, rather than resulting from cell lysis."

And conclude

"...the discovery is fascinating and will undoubtedly lead to the identification of novel defence strategies and secretion processes."

Read all comments in full.

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F1000 Biology Reports

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In this study, the effect that vision of the body has on the perception of pain was investigated…MORE
Selected by | Alumit Ishai (University of Zurich, Switzerland)

Must Read
F1000 Factor 6.0

Visually induced analgesia: seeing the body reduces pain.
Longo MR et al. *J Neurosci* 2009 Sep 30 **29**(39):12125-30

I found this article interesting because I was very surprised that loss of central tolerance to a single antigen was sufficient to cause autoimmune diabetes in a mouse strain not genetically prone to this disease…MORE
Selected by | Thomas Kay (St. Vincent's Institute of Medical Research, Australia)

Thymus-specific deletion of insulin induces autoimmune diabetes.
Fan Y et al. *EMBO J* 2009 Sep 16 **28**(18):2812-24

Cleaving human genomic DNA just once is quite a feat. The authors have accomplished this feat using a highly sequence-selective chemical approach…MORE
Selected by | Scott K Silverman (University of Illinois at Urbana-Champaign, USA)

Site-selective scission of human genome by artificial restriction DNA cutter.
Ito K et al. *Chem Commun (Camb)* 2009 Nov 21 (43):6542-4

The authors suggest the novel idea that the dynamically unbalanced kinase activity contributions of Akt1 and Akt2 modulate cancer malignancy via differential regulation of microRNA-200 (miR-200), and, thus, the authors possibly present a potential new clinical target for the inhibition of cancer progression.…MORE
Selected by | Gongda Xue and Brian Hemmings (Friedrich Miescher Institute, Switzerland)

MicroRNAs differentially regulated by Akt isoforms control EMT and stem cell renewal in cancer cells.
Iliopoulos D et al. *Sci Signal* 2009 **2**(92):ra62

The developmental origin of Merkel cells has long been debated. This report conclusively demonstrates the developmental origin of these unique skin cells…MORE
Selected by | Aislyn M Nelson and Ellen A Lumpkin (Baylor College of Medicine, USA)

Epidermal progenitors give rise to Merkel cells during embryonic development and adult homeostasis.
Van Keymeulen A et al. *J Cell Biol* 2009 Oct 5 **187**(1):91-100

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