

**EDITORS-IN-CHIEF**

Kevin J Tracey, MD  
*The Feinstein Institute for Medical Research  
Manhasset, NY, USA*

Anthony Cerami, PhD  
*Kenneth S Warren Laboratories  
Tarrytown, NY, USA*

**EDITORIAL STAFF**

Christopher J Czura  
*Executive Editor  
The Feinstein Institute for Med  
Manhasset, NY, USA*

Margot Gallowitsch-Puerta  
*Managing Editor  
The Feinstein Institute for Med  
Manhasset, NY, USA*

Veronica J Davis  
*Assistant Editor  
The Feinstein Institute for Med  
Manhasset, NY, USA*

## Podcast Transcript Top 5 Mol Med Papers Cited in 2008

Hello *Mollie Medcast* listeners and welcome back. *Mollie Medcast* is the podcast for the biomedical journal, *Molecular Medicine*. My name is Margot Puerta. I'm the managing editor here at *Molecular Medicine* and your host for this podcast episode. Since it's the end of the year, we have a special episode this week. Instead of reviewing newly published manuscripts, we'll be looking back at the top five *Molecular Medicine* papers cited during the year 2008.<sup>1</sup> And, to help me with the countdown, I've asked Mol Med's assistant editor, Veronica Davis, to join us.

[Margot:] Hi Veronica and thanks for joining me on the *Mollie Medcast*.

[Veronica:] Thanks for having me.

Before we get to those papers, I would like to review our mission. *Molecular Medicine's* mission is to publish novel work that's concerned with understanding the pathogenesis of disease at the molecular level, which may lead to the design of specific molecular tools for disease diagnosis, treatment, and prevention. All of our manuscripts are available online, free without login or passwords, on our website, [www.molmed.org](http://www.molmed.org).

Okay, so here we go, off to the top cited papers in 2008. We're going to go in reverse order down to number one, David Letterman style:

#5: Association of STAT4 with rheumatoid arthritis in the Korean population by Dr. Lee, published in 2007.

#4: Insulin signaling and the regulation of glucose transport by Dr. Chang, published in 2004.

#3: The molecular mechanism of autophagy by Dr. Wang, published in 2003.

#2: Differentiation of human embryonic stem cells into embryoid bodies comprising the three embryonic germ layers, by Dr. Itskovitz-Eldor in 2000.

And the *Molecular Medicine* paper that received the most citations in the year 2008 was:  
Erythropoietin therapy for acute stroke is both safe and beneficial, by Dr. Ehrenreich published in 2002.

### **#5 Association of STAT4 with Rheumatoid Arthritis in the Korean Population**

This primary research paper was published in *Molecular Medicine* in 2007, in our September-October Issue (Vol 13 No 9-10). The lead author is Hye-Soon Lee and she collaborated with researchers from The Feinstein Institute in New York, Hanyang University College of Medicine in South Korea, and The National Institute of Arthritis and Musculoskeletal and Skin Diseases in Maryland. The paper discusses risk genes for rheumatoid arthritis, which is abbreviated RA. A study in the North American White population documented the association of a common STAT4 haplotype with risk for RA and systemic lupus erythematosus. Dr. Lee examined this finding in the Korean population and performed a case-control association study. Sixty-seven single nucleotide

polymorphisms, or SNPs, were genotyped within the STAT1 and STAT4 regions in 1123 Korean patients with RA and 1008 ethnicity-matched controls. The most significant four risk SNPs are identical with those in the North American study. All four SNPs have modest risk for RA susceptibility and a common haplotype defined by these markers carries significant risk for RA in Koreans. Unlike several other risk genes for RA, a haplotype of the STAT4 gene shows consistent association with RA susceptibility across Whites and Asians, suggesting that this risk haplotype predated the divergence of the major racial groups.

#### **#4 Insulin Signaling and the Regulation of Glucose Transport**

This paper by Drs. Chang, Chiang and Saltiel was published by Mol Med in 2004 (Vol 10 No 7-12) out of the Life Sciences Institute, Departments of Internal Medicine and Physiology, University of Michigan in Ann Arbor. This manuscript is a review paper which in 2004 we called "In Overview". And in it the authors discuss insulin and the glucose transporter Glut4. Insulin promotes storage and synthesis of lipids, proteins, and carbohydrates and inhibits their breakdown and release into circulation. One of the first steps in increasing or utilizing energy storage involves regulated transport of glucose into the cell. This is mediated by the glucose transporter, Glut4. Insulin increases glucose uptake by enriching the concentration of Glut4 proteins in the plasma membrane. Glut4's cellular location is governed by a tightly regulated process of recycling. Dr. Chang and colleagues review the molecular basis for these events and the signaling processes which control them.

#### **#3 The Molecular Mechanism of Autophagy**

This is the third most cited Mol Med paper in 2008 by authors Chao-Wen Wang and Daniel Klionsky. It was published in 2003 in our March-April issue (Vol 9 No 3-4) and is also an "In Overview" paper. The title is self-explanatory, The Molecular Mechanism of Autophagy. I did a quick check on Wikipedia for autophagy and the first line under Autophagy said, "For animals eating themselves, see self-cannibalism"<sup>2</sup> which is I guess, one way to look at it. Autophagy, as we know, is trafficking pathway. It's highly regulated by environmental conditions. During autophagy, parts of the cytoplasm are sequestered into a double-membrane autophagosome and delivered to a degradative organelle for breakdown and recycling. In yeast it's the vacuole and in mammalian cells it's the lysosome. Autophagy is induced under starvation conditions and in mammalian cells is also invoked in response to specific hormones. In yeast, under nutrient-rich conditions, a constitutive biosynthetic pathway, termed the cytoplasm to vacuole targeting pathway or Cvt, utilizes most of the same molecular machinery and topologically similar vesicles for the delivery of the resident hydrolase aminopeptidase I to the vacuole. In this review, Drs. Wang and Klionsky focus on the yeast system, which has provided most of the insight into the molecular mechanism of autophagy and the Cvt pathway, as well as highlight their (at the time) most recent additions to knowledge of both pathways.

#### **#2 Differentiation of Human Embryonic Stem Cells in Culture**

This primary research article was written by Dr. Joseph Itskovitz-Eldor and colleagues from the Rambam Medical Center and the Institute of Life Sciences, both in Israel. It was published by Mol Med in 2000 in the February issue (Vol 6 No 2). Producing replacement tissues for therapeutic use remains an elusive goal of biomedical engineering. It has been complicated by the inability to culture totipotent cells. Studies of mouse embryonic stem cells show that these cells are highly pluripotent and can differentiate into all of the embryonic cell types. Primate studies, however, have encountered difficulties. Embryonic stem cells derived from the marmoset, despite being morphologically well organized, differentiated into inconsistent and asynchronous embryoid bodies. The differentiation of rhesus embryonic stem cells was disorganized and embryoid bodies formed no distinct vesicular structures. The recent availability of human embryonic stem cell lines, derived from human embryos produced by in vitro fertilization, has led to an increased interest in human embryonic development. In this article, Dr. Itskovitz-Eldor and colleagues presented their findings on the differentiation of human embryonic stem cells into embryoid bodies in suspension in vitro. The cells developed new functions, as evidenced by the appearance of pulsing muscle cells. The authors suggest that these findings may make it possible to differentiate human embryonic stem cells into specific lineages, which can serve as a source of cells for tissue replacement and will allow the study of human embryonic development in vitro.

And, the #1 cited *Molecular Medicine* paper during the year 2008,

### **Erythropoietin Therapy for Acute Stroke is both Safe and Beneficial**

This article describes the results of a clinical trial conducted by Dr. Hannelore Ehrenreich, now one of our own Contributing Editors. Erythropoietin, abbreviated EPO, protects neurons from hypoxic/ischemic injury and the objective the trial was to study the safety and efficacy of recombinant human EPO [rhEPO] for treatment of ischemia in humans. The trial was divided into two stages, one reviewing safety and one reviewing efficacy. For safety, 13 patients were given recombinant human EPO i.v. once daily for the first 3 days after stroke. In the efficacy portion, a double-blind randomized proof-of-concept trial included 40 patients receiving either recombinant human EPO or saline. No safety concerns were identified and additional results indicated that recombinant human EPO given i.v. does reach the brain. In the efficacy trial, results indicated that recombinant human EPO treatment was associated with an improvement in follow-up and outcome scales. A strong trend for reduction in infarct size in recombinant human EPO patients as compared to controls was observed by MRI. Dr. Ehrenreich concluded the recombinant human EPO was well-tolerated and a larger scale clinical trial was warranted.

That's it for this week's episode of *Mollie Medcast*. We hoped you enjoyed the brief time travel backwards. As always, you can find these papers, free, without login or passwords, on our website, [www.molmed.org](http://www.molmed.org) that's [www.m-o-l-m-e-d.org](http://www.m-o-l-m-e-d.org).

This podcast is available on our website but is also up in iTunes. Just type "Mollie Medcast" in the search bar. *Molecular Medicine* is published bimonthly by The Feinstein Institute for Medical Research. From Long Island, New York, this is Veronica, thanks for having me, and thanks for listening!

Written and Produced by Margot Puerta  
Managing Editor, *Molecular Medicine*

Production Assistant: Veronica J Davis  
Assistant Editor, *Molecular Medicine*

Music: Opuzz.com

References:

1. Web of Science, Thomson Reuters.
2. <http://en.wikipedia.org/wiki/Autophagy> Accessed December 30, 2008.