

involves other cytokines, including IL-13 and IL-4, which also recruit eosinophils into the airways.

Although the exact number of severe-asthma patients eligible for IL-5 inhibitors is not known, there is an unmet need because these patients undergo more treatments and hospitalizations, contributing to greater medical costs compared to the larger number of milder-asthma patients, says Kian Fan Chung of the National Heart and Lung Institute in London. “The approval of Nucala represents a hope for those patients with severe eosinophilic asthma experiencing frequent exacerbations.” The market potential for all three antibodies is \$2.9 billion by 2020 predicts Richard Parkes, senior analyst at Deutsche Bank in the UK. Parkes estimates there are about 500,000 uncontrolled, severe-asthma patients in the US, of which about half have eosinophilic disease.

Nucala, which is administered subcutaneously every four weeks, has a wholesale acquisition cost of \$2,500 per single-use vial. “The market has potential to grow significantly

but one of the major issues is defining which patients should be on an expensive biologic therapy when the vast majority will respond to corticosteroids,” says Parkes. Nair agrees. The majority of patients enrolled in these trials were not well managed, as evidenced by the 50% improvement in exacerbations in the placebo arms of these clinical trials, says Nair, who would like to see only those who truly cannot be managed with current therapy receive the expensive biologics. The rest, he says, just need to be better monitored for health and compliance, and given better access to medication.

There is a still larger opportunity for IL-5 inhibitors in a wider indication: eosinophilic chronic obstructive pulmonary disease (COPD). Both Nucala and benralizumab are currently in phase 3 for the lung disease. According to Yao, about one-third of those with COPD have elevated eosinophil counts. GSK is also investigating their antibody Nucala for use in eosinophilic granulomatosis with polyangiitis. “There are several other indications. You could also imagine [IL-5 antibodies] could be effective in patients with nasal polyps or even eosinophilic esophagitis,” says Yancey.

Anna Azvolinsky *New York*

First Rounders Podcast:

James Wilson

James Wilson is the director of the Gene Therapy Program at the University of Pennsylvania. He is also a founder and chief scientific advisor at RegenxBio, as well as founder and chairman of the scientific advisory council at Dimension Therapeutics. Wilson's conversation covers his love of motocross racing, the triumphs and tribulation of gene therapy (including the Jesse Gelsinger tragedy) and the future of drug pricing.

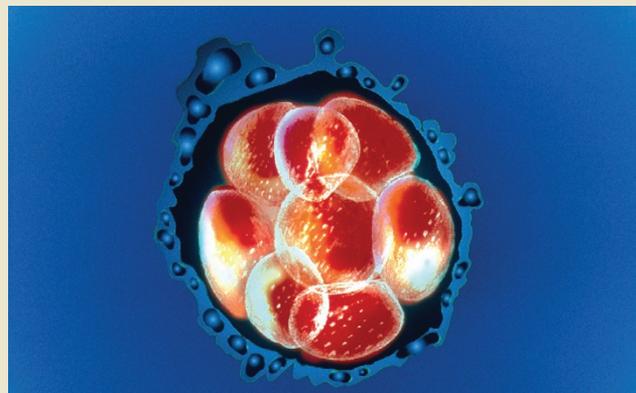
<http://www.nature.com/nbt/podcast/index.html>



Go-ahead for human genome editing with caveats

A global summit to discuss the future of human gene editing was convened by the US National Academy of Sciences and US National Academy of Medicine; the UK's Royal Society and the Chinese Academy of Sciences in December. The International Summit on Human Gene Editing, chaired by David Baltimore, president emeritus at the California Institute of Technology in Pasadena, ran December 1–3 in Washington, DC, bringing together almost 500 ethicists, legal experts, biomedical researchers and advocacy groups. The meeting was prompted by the April publication by Chinese researchers who used the gene editing technology CRISPR-Cas9 to modify a gene in a nonviable embryo (*Prot. Cell.* **6**, 363–372, 2015). UK funding agencies were first to issue a statement supporting human germline editing in research (*Nat. Biotechnol.* **33**, 1118–1119, 2015).

After three days of discussion over where to draw the line between acceptable and unacceptable, the organizers issued a position statement with four main conclusions (<http://www8.nationalacademies.org/onpinews/newsitem.aspx?RecordID=12032015a>). First, given the potential benefits from these technologies, basic and preclinical research should proceed, subject to legal and ethical rules and oversight. This may include early human embryos or germline cells but which should not be used to establish a pregnancy. The second ruling applies to gene editing in somatic cells, for example, gene editing red blood cells to treat sickle cell anemia. Such clinical uses affect only the individual who receives them and so can proceed under existing regulatory frameworks and should be allowed to continue. When gametes or embryos are altered by gene editing, much uncertainty surrounds safety, efficacy and societal issues. As a result, the third statement deems it irresponsible to proceed for now but the issue should be revisited regularly as scientific knowledge advances and societal views evolve. Finally, the summit agreed that although each national



The 8-embryo stage in an embryo.

authority ultimately regulates activities under its jurisdiction, there is a need for ongoing discussions held by an international forum that brings in a wide range of nations and expertise, including the general public, regulators, industry and faith leaders.

Among those attending were biomedical researchers Paul Berg, Stanford University School of Medicine; George Daley, Boston Children's Hospital and Dana-Farber Cancer Institute in Boston; Jennifer Doudna, University of California, Berkeley; Eric Lander, the Broad Institute of Harvard and MIT in Cambridge, Massachusetts; Robin Lovell-Badge, Francis Crick Institute, London; Duanqing Pei, Chinese Academy of Sciences, Guangzhou; Adrian Thrasher, University College London Institute of Child Health, London; Ernst-Ludwig Winnacker, University of Munich; and ethicists Françoise Baylis, Dalhousie University, Nova Scotia; and Pilar Ossorio, University of Wisconsin and Morgridge Institute for Research, Madison.