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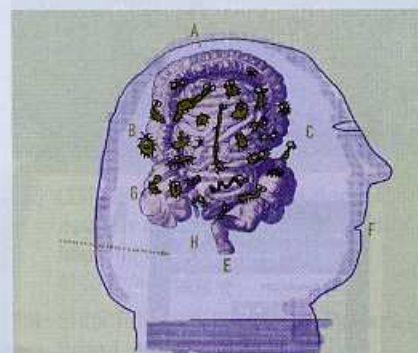
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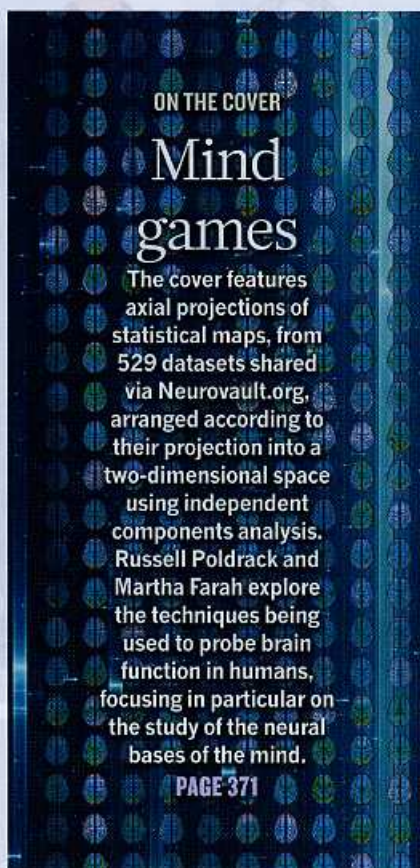
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448 **NEUROSCIENCE** Inhibition of Gli1 mobilizes endogenous neural stem cells for remyelination  
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453 **CANCER** Alternative transcription initiation leads to expression of a novel *ALK* isoform in cancer  
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458 **ADDENDUM** Plio-Pleistocene climate sensitivity evaluated using high-resolution  $\text{CO}_2$  records  
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458 **CORRIGENDUM** Carbonic anhydrases, *EPF2* and a novel protease mediate  $\text{CO}_2$  control of stomatal development  
C B Engineer et al.

RUSSELL POLDRACK & KELLY KRAUSE (SOURCE: NEUROVAULT.ORG)



## PRECISION MEDICINE

### REVIEWS

#### 336 Building the foundation for genomics in precision medicine

The goal of precision medicine is to finely tailor the practice of medicine to the individual to provide optimal treatments for patients. For its implementation to be effective, a new infrastructure is required that brings together patients, clinicians, clinical laboratories and researchers. Samuel Aronson and Heidi Rehm explore how this precision-medicine 'ecosystem' is being built, as well as the development of the infrastructure and mechanisms that are necessary to store, share and analyse genetic and clinical data as a foundation for precision medicine.

Samuel J. Aronson & Heidi L. Rehm

#### 343 Pharmacogenomics in the clinic

Pharmacogenomic studies seek to identify genetic variation that influences how an individual responds to a particular drug. Mary Relling and William Evans review progress in pharmacogenomic discovery efforts, as well as the selection of gene-drug pairs that are considered to be actionable such that genetic-test results could guide modulation of the drug regimen or the use of an alternative treatment. They also consider the application of both reactive and pre-emptive pharmacogenomics testing and the steps — including the development of guidelines for interpreting and translating results into actionable recommendations — that are needed to bring such testing into the clinic to support evidence-based treatment.

Mary V. Relling & William E. Evans

#### 351 Gene therapy returns to centre stage

Gene therapy offers the potential to treat a disease at its genetic roots. However, the challenges faced during its implementation include difficulties in using gene transfer to safely deliver a therapeutic molecule into targeted cells. Luigi Naldini reviews progress in gene therapy, including recent promising results from clinical trials that show increased efficacy and safety in the treatment of a number of severe inherited diseases. These successes

have been facilitated by technical improvements in vector design as well as by targeted genome editing.

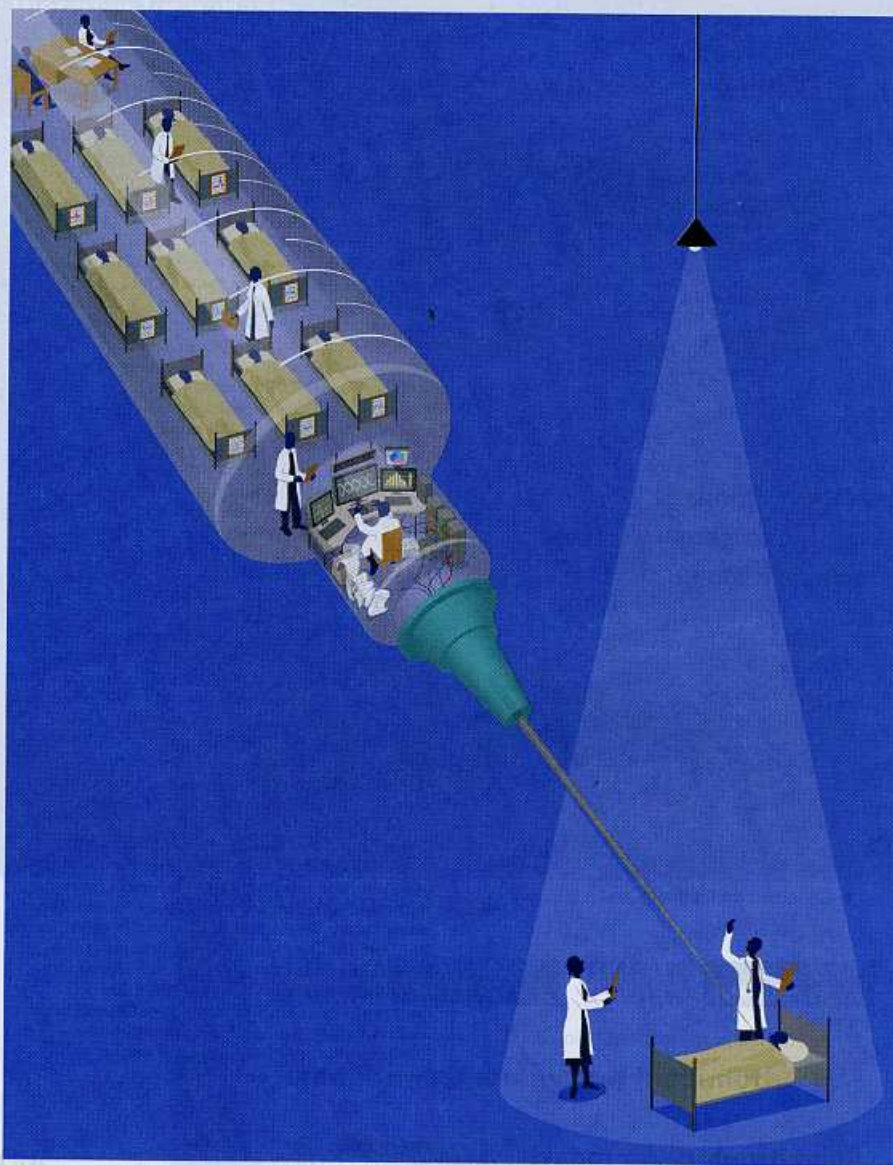
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#### 361 Patient-centric trials for therapeutic development in precision oncology

Improved characterization of the molecular pathology of a wide range of cancers is becoming possible through genomic studies, which allows the development of treatments that target specific molecular subclasses

of tumours. Andrew Biankin and colleagues review progress that has been achieved in targeted-drug development for oncology by placing the patient at the centre of this process. This includes the development of innovative clinical-trial designs that take into account tumour subclasses and offer advances in matching the right trial to the right patient.

Andrew V. Biankin, Steven Piantadosi & Simon J. Hollingsworth



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