

IN BRIEF

GENE THERAPY**Diluting the immune response with decoys**

Adeno-associated virus is one of the main vectors used in gene therapy. However, its success in humans has been limited owing to the immune response it stimulates. In this paper, the authors show that in non-human primates and mice, the neutralizing antibodies that target the vectors can be adsorbed by empty capsids that are delivered with the vectors, hence improving gene delivery. They also enhanced the safety of this approach by generating an empty capsid mutant that cannot enter a cell. The capsid/vector ratio can be optimized for future delivery.

ORIGINAL RESEARCH PAPER Mingozzi, F. *et al.* Overcoming preexisting humoral immunity to AAV using capsid decoys. *Sci. Transl. Med.* <http://dx.doi.org/10.1126/scitranslmed.3005795> (2013)

TRANSCRIPTOMICS***In situ* RNA-seq**

Analysis of gene expression in tissues is normally carried out in homogenized samples or isolated single cells. These authors have developed a method to sequence RNA directly in preserved tissue and cells. This method amplifies and sequences RNAs by ligation *in situ*, and this is combined with an automated imaging pipeline for sequence readouts. Thus, the location of the transcript is maintained within the tissue. The authors demonstrated the application of this technique in breast cancer tissue by identifying point mutations and carrying out gene expression profiling.

ORIGINAL RESEARCH PAPER Ke, R. *et al.* *In situ* sequencing for RNA analysis in preserved tissue and cells. *Nature Methods* <http://dx.doi.org/10.1038/nmeth.2563> (2013)

COMPLEX DISEASE**Meta-analysis for rare variants**

Meta-analyses — which combine large numbers of cases from multiple studies in order to increase the power to detect disease–gene associations — are increasing in popularity in human genetic studies. Meta-analyses are, however, challenging for rare variants. As they are currently carried out by aggregating variants at the gene level to enrich for association signals, it is difficult to analyse rare variants for a number of reasons. To overcome these issues, Hu *et al.* have developed an approach to perform meta-analyses on rare variants by combining the results of single variant analyses. They successfully applied this method to data from previous studies to identify rare and common variants associated with height.

ORIGINAL RESEARCH PAPER Hu, Y.-J. *et al.* Meta-analysis of gene-level associations for rare variants based on single-variant statistics. *Am. J. Hum. Genet.* <http://dx.doi.org/10.1016/j.ajhg.2013.06.011> (2013)

EVOLUTION**Genetic hitch-hiking prevalence**

Here, the authors performed an experimental evolution of 40 replicate *Saccharomyces cerevisiae* populations growing in rich medium for 1,000 generations. They sequenced the genomes of these yeast cells and found that genetic hitch-hiking is prevalent — mutations arise and are transmitted together, as one is selected for and the other hitch-hikes along. These mutational cohorts compete with each other within the population and sequence evolution is a result of such hitch-hiking and interference. Such a phenomenon could allow populations to rapidly respond to environmental variations.

ORIGINAL RESEARCH PAPER Lang, G. I. *et al.* Pervasive genetic hitchhiking and clonal interference in forty evolving yeast populations. *Nature* <http://dx.doi.org/10.1038/nature12344> (2013)