misincorporations, a highly sensitive and specific method.

The new study demonstrates that next-generation sequencing data can, in some cases, erroneously give the impression of widespread internal modifications in mRNA. Although m^6A and pseudouridine are well-documented epitranscriptomic modifications, and their mapping can be performed reliably[10,11], the validity of newer modification maps is unclear, because the modifications were mapped from sequencing data but not biochemically validated. A recent study[12] of the mammalian transcriptome mapped approximately 3,500 nucleotides that contain methyl groups on the ribose part of the molecules. However, subsequent reanalysis showed that the key sequence motifs discovered in this study matched those of 'primer' sequences used to generate complementary DNA, a common sequencing artefact[13].

Rigorous criteria are therefore needed to validate the results of modified-nucleotide mapping studies. Foremost among these is direct biochemical validation of modifications in target mRNAs. Additional criteria should include confirmation that a modification site is seen in separate mapping studies using independent, modification-specific antibodies. If the modified nucleotide causes mutations during reverse transcription, then these mutations should also be used to verify mapping data. Lastly, experiments in which the modification-synthesizing enzyme is deliberately depleted in cells can further demonstrate the specificity of a mapping experiment, as Safra *et al.* have shown. ■

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50 Years Ago

Metropolitan areas suffer from too many people, too much congestion, problems of pollution and a scarcity of chlorophyll and sunlight … Continual efforts must be made to prevent unnecessary concentration of activities in London, particularly in the central area … This is where technology comes in. With the improvements now in prospect for the decades ahead, there is good reason to re-examine the assumptions on which the doctrine of counter-magnet cities has been based. Specifically, it would be good to know how far it may be possible to give people who live and work in satellite cities a sense that they are nevertheless a part of the metropolis … Why, for example, should not the city now certain to emerge on the Solent be deliberately linked with London by fast train services and cheap telephone circuits in such a way that it would seem no farther away than the outer suburbs of the metropolitan sprawl?
From *Nature* 11 November 1967

100 Years Ago

Victory in the air … depends on two sets of factors — tactical and technical … To secure a good tactical position a machine must possess good technical factors; for instance, good armament is useless unless a machine is fast enough to be able to challenge the enemy to battle … In the early days the importance of the mastery of the air had not been fully appreciated, and aerial combats were rare. The chief use of aeroplanes was to obtain information as to the enemy's position … Early aerial fights were generally ineffective, and resulted in a few bullet-holes in the wings, mainly owing to the difficulties of aim and the small quantity of ammunition carried.
From *Nature* 8 November 1917

CHEMICAL BIOLOGY

Organic dyes for deep bioimaging

Small-molecule organic dyes that fluoresce in the short-wave infrared region of the spectrum could improve the resolution of *in vivo* bioimaging methods. Such dyes have now been made by adapting those that fluoresce visible light.

MARTIN J. SCHNERMANN

Fluorescence-based imaging methods have transformed the way that scientists visualize and interpret biological events. An enduring goal is to make fluorescence imaging broadly useful in complex physiological settings, especially for clinical applications. One strategy is to use fluorescence wavelengths between 1,000 and 2,000 nanometres — the short-wave infrared (SWIR) region of the electromagnetic spectrum. But organic molecules that absorb and emit these wavelengths are needed to realize the full potential of SWIR imaging[1]. Writing in *Angewandte Chemie*, Cosco *et al.*[2] report the brightest known organic small-molecule dyes that absorb and emit light at wavelengths greater than 1,000 nm.

Red light is preferentially transmitted through tissue — which is why your hand lights up red when you hold a torch behind it. To take advantage of this property, there have been substantial efforts to develop probes and *in vivo* imaging techniques that use far-red and near-IR wavelengths (650–1,000 nm).

However, imaging in the SWIR range offers important benefits for *in vivo* applications, compared with that in the far-red and near-IR, for two main reasons. First, SWIR produces less autofluorescence — light emitted naturally by biological structures that have previously absorbed light — so that images are produced against a nearly black background. Second, light scattering caused by particulate matter generally decreases with longer wavelengths. A theoretical study[3] has predicted a 100- to 1,000-fold improvement in image resolution at centimetre depths of tissue when imaging in the SWIR range (1,350 nm),