NATURE

50 Years Ago

The Liberal conference which took place last week afforded the now familiar sight of the Young Liberals adopting a more radical and militant approach than that of the parent body, and being subsequently chastised for it. But the motion which had the greatest bearing on science and technology, on European unity, was largely their work. This motion commits the Liberal Party to press not only for entry into the EEC but also for a "United States of Europe" with common economic, technological and foreign policies. The Liberals see this as the only effective way to combat the increasing American dominance of European technology and consumer markets … The motion was carried by an overwhelming majority, and this makes the Liberal Party the foremost advocate of joining the Common Market among the political parties.
From *Nature* 27 September 1969

100 Years Ago

Dr. Victor E. Shelford writes in the *Scientific Monthly* … on the general question of the waste involved in the discharge of domestic and industrial sewage into the sea and rivers. Experimental methods for testing the effect on fishes of various substances in solution have been devised … The sensibility of fish to such compounds as occur in waste material is thus shown to be greater than has hitherto been supposed, thus an increase in carbon dioxide of 2 c.c. in one litre above the normal content caused the turning-away reaction. A low oxygen content was also detrimental, and this was usually found to accompany a high carbon dioxide content. The waste substances resulting from gas-production works and from munitions processes were also studied, and it was shown that these substances … had very marked effects on fish-life.
From *Nature* 25 September 1919

When the authors superimposed an available structure of a pMHC bound to a TCRαβ heterodimer onto their TCR structure, the TCRαβ heterodimers were similar in both structures. This is unsurprising, because force application is probably the major cause of structural changes driving TCR subunit rearrangements, and these structures were obtained in the absence of force, and thus capture a compact state of the TCRαβ heterodimer. The force-based TCR–pMHC recognition process differs from typical receptor–ligand interactions such as antibody–antigen interactions, which are force-independent. Harnessing energy for mechanosensing from cellular motions could explain how, unlike in force-independent interactions, TCRs can discriminate so sensitively between very similar antigens, differing by just one amino acid.

It has been suggested that the subunit rearrangements that occur when force is applied to the TCR might foster CD3 dimer dissociation, starting with CD3ζζ, and that this contributes to T-cell activation[8]. The authors' structure confirms that CD3ζζ dissociation would indeed cause changes to the TCR structure in the transmembrane region.

Dong and colleagues' work provides a basis for future studies. Could structures of other αβ-type TCRs of defined antigen specificities, with or without the relevant pMHC, be obtained? Might it be possible to obtain high-resolution structures of the transmembrane segments of a TCR in a natural lipid-membrane environment to visualize the cytoplasmic tails of TCR proteins? Could conformations of the TCR complex under the application of force be imaged if new structural-analysis methods are developed?

Given the importance of the TCR for understanding immune-cell function and the use of T cells in immunotherapy to tackle cancer, information about TCR structure might bring improvements in TCR design for medical purposes. Dong and colleagues' work is an urgent summons to immunologists interested in tumour biology and to others to consider bioforces when assessing T cells *in vitro* to gauge the potential of their TCRs *in vivo*. Great opportunities lie ahead to make more progress in developing high-quality TCRs for clinical use. ■

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CONDENSED-MATTER PHYSICS

X-rays glimpse solid hydrogen's structure

Little was known about the properties of hydrogen under extreme pressure. Experiments now reveal key details about the arrangement of molecules in several of the element's high-pressure phases. **SEE LETTER P.558**

BARTOMEU MONSERRAT & CHRIS J. PICKARD

Hydrogen is the most abundant element in the Universe. Our knowledge of celestial bodies such as the Sun, which is about 75% hydrogen[1], relies on understanding the properties of this element at extreme temperature and pressure. Replicating these conditions in the laboratory is exceptionally challenging, and even the structure of high-pressure phases of hydrogen at low temperatures has been an open question. On page 558, Ji *et al.*[2] report experiments that probe this structure at unprecedented pressures, revealing a hexagonal close-packed arrangement of molecules.

The simplicity of the hydrogen atom, which comprises a single proton and a single electron, does not prevent the high-pressure phases of the element from being rich and complex. Hydrogen is an electrical insulator at ambient conditions, but becomes a metal under extreme compression[3] — a state that could, for example, help to generate Jupiter's magnetic field. Additionally, theoretical work suggests