

1990.⁹ And it is of very high affinity, making it active in the ng/mL range, exactly as requested by McLachlan and Rapoport. The remaining criteria—that the monoclonal should be inactive after preadsorption with the TSH receptor but active after fine purification, and that expression of recombinant protein derived from the heavy-chain and light-chain genes should also produce a thyroid-stimulating immunoglobulin—have not been addressed in the current report, but seem likely to be met.

So is the final proof of the existence of thyroid-stimulating immunoglobulin after a journey of 47 years of anything more than academic interest? Almost certainly the answer is yes. First, it might lead to a new generation of assays for thyroid-stimulating immunoglobulin in which competition for labelled TSH is replaced by competition for specific monoclonal antibodies.¹⁰ If a sensitive assay can be developed, it should have close to 100% specificity for Graves' disease and replace all other antibody tests, such as antithyroid peroxidase and antithyroglobulin, in this condition. Second, it should finally allow us to understand how such antibodies, even in the monomeric Fab form, can activate the TSH receptor. Such understanding of the biology of glycoprotein-hormone receptors may lead to new small-molecule agonists and antagonists not only for thyroid disease but also for hypogonadism and infertility (via the closely related receptors for luteinising and follicle-stimulating hormones). And it may prove possible to clone a potent human TSH-receptor-blocking antibody which might provide a rapid initial treatment for thyrotoxicosis. Third, the finding may lead to a better understanding of the pathogenesis of Graves' disease. How is it that the spontaneous development of such agonist antibodies, unique in autoimmune diseases, occurs so frequently (almost 1 in 100 of the population)? Does the agonist activity itself, once it appears, promote autoimmunity in a positive feedback loop? Most intriguingly, cloning of agonist TSH-receptor autoantibodies might reveal antibodies that contribute to thyroid eye-disease, the most mysterious manifestation of Graves' disease, and perhaps lead to inhibitors for these antibodies. And finally, agonist antibodies may prove a useful therapeutic agent in their own right, such as to enhance iodine-131 uptake in thyroid cancers. Many of the holy grails of biological science, from the structure of DNA to the nature of the T-cell antigen receptor, have been found. Thankfully, once in hand, they change into pointers to the many more waiting to be discovered.

Work in the author's laboratory is supported by Goldshield Pharmaceuticals.

Colin M Dayan

University Research Centre for Neuroendocrinology,
Department of Medicine, University of Bristol, Bristol Royal Infirmary,
Bristol BS2 8HW, UK
(e-mail: Colin.dayan@bris.ac.uk)

- 1 McLachlan SM, Rapoport B. Monoclonal, human autoantibodies to the TSH receptor—the Holy Grail and why are we looking for it? *J Clin Endocrinol Metab* 1996; **81**: 3152–54.
- 2 Adams DD, Purves HD. Abnormal responses in the assay of thyrotropin. *Proc Univ Otago Med Sch* 1956; **34**: 11–12.
- 3 Roitt IM, Ling NR, Doniach D, et al. Autoantibodies in Hashimoto's disease (lymphadenoid goitre). *Lancet* 1956; **2**: 820–22.
- 4 Parmentier M, Libert F, Maenhaut C, et al. Molecular cloning of the thyrotropin receptor. *Science* 1989; **246**: 1620–22.
- 5 Nagayama Y, Kaufman KD, Seto P, et al. Molecular cloning, sequence and functional expression of the cDNA for the human thyrotropin receptor. *Biochem Biophys Res Commun* 1989; **165**: 1184–90.

- 6 Sanders J, Jeffreys J, Depraetere H, et al. Thyroid stimulating antibodies. *Thyroid* 2002; **12**: 1043–50.
- 7 Ando T, Latif R, Pritsker A, et al. A monoclonal thyroid stimulation antibody. *J Clin Invest* 2002; **110**: 1667–74.
- 8 Costagliola S, Fransen JD, Bonomi M, et al. Generation of a mouse monoclonal TSH receptor antibody with stimulating activity. *Biochem Biophys Res Commun* 2002; **299**: 891–96.
- 9 Weetman AP, Yateman ME, Ealey PA, et al. Thyroid-stimulating antibody activity between different immunoglobulin G subclasses. *J Clin Invest* 1990; **86**: 723–27.
- 10 Costagliola S, Vassart G. Monoclonal antibodies with thyroid stimulating activity, at last. *Thyroid* 2002; **12**: 1039–41.

Medicine, the arts, and the humanities

“Knowledge is limited. Imagination encircles the world”

Albert Einstein¹

Medical and scientific developments and innovations, with their attendant social and ethical consequences, rely on a multidisciplinary involvement of science and humanities. The practice of medicine furthermore involves knowledge and skills based on education and experience in both. The arts and humanities can also contribute ways of reconceptualising medicine itself. Stephen Pattison² and Robin Downie³ recently discussed what medical humanities is, what it might and might not be able to do, and what they hope it will not do. “Medicine and health . . . are human concerns in the widest sense”, according to Pattison. Study of the humanities may not be able to make clinicians more humane, says Downie, but it can foster a depth of human and humane understanding, knowledge, and experience.

Arts and humanities approaches are intrinsic to society's understanding of medicine. Bodies, minds, emotions, and relationships are explored and expressed through the arts and humanities as well as science; academically and intellectually, as well as personally. Do the sciences not also rely for their effectiveness on understanding, critical analysis, meaning, discernment, interpretation, visualisation, and creativity, all fostered by subjects traditionally considered to be based on humanities and arts?⁴

The humanities are reflective and disciplined inquiries that involve the recording and interpretation of the range of human experience.⁵ The medical humanities encompass history, literature, philosophy, ethics, theology, sociology, anthropology, and possibly law. These disciplines offer a multifaceted view. They value the aesthetic as well as reason, focus on meaning as well as emotion, and explore ambiguity, uncertainty, and complexity as well as theoretical lucidity. They offer understanding through synthesis as well as analysis—all integral elements of medicine. Educationally, the medical humanities can enable and develop critical conceptualisation and analysis of personal and professional values, and the reflexive and reflective capacities of empathy, collegiality, and teamwork. All these approaches can foster critical evaluation and effective understanding of patients' unique narratives and needs.^{6,7}

Medical consultation is a complex communication, both verbal and physical, involving issues of risk, values, and ethics. The clinician brings tacit understandings and personal experience, as well as professional expertise and knowledge. Patients bring broken bodies or minds. But often more than the body or mind is broken: patients' understanding of themselves and the

certainty of their lives is often also disrupted and disturbed. Together, clinician and patient can co-construct a curative and healing narrative that involves medical and healthcare interventions, and mental and emotional understandings, which can help the patient constructively rebuild their life, or prepare for death.⁸

A recent UK Government directive states that: "The greatest challenges for society . . . are all ones in which the arts and humanities, and science and technology need each other . . . [Medical] education is about understanding and imagination, as well as training and skills".⁹ Medical humanities is responding fast,¹⁰ and all involved in the field are asked to join a dialogue of its nature and effects.¹¹

Medical practitioners work with people through the biggest dramas of life: birth, death, disablement, and life-altering disease. Such work also brings anxiety, harassment, frustration, and disillusionment. Some of these intimate and privileged encounters inevitably include extraordinary comedy as well as tragedy. The treatment and care of ill and often distressed people constantly confronts practitioners with fundamental questions about the meaning and sanctity of life and the problem of suffering. A sound grounding in the arts and humanities can enable an effectively critical, humane, and ethical response.¹²

For the medical humanities to continue to be of real use, they need to retain an intrinsic value, and not become "instrumental technologies"² (as a mere means to promoting, for example, communication skills). An interdisciplinary breadth, inclusivity, vigour, and spirit of intellectual inquiry is needed. Pattison² and Downie³ also caution against pitfalls into which medical ethics has fallen: "routinisation, exclusivism, narrowing, specialisation, and professionalisation",² which could result in the elimination of "radically different approaches to the big questions and issues of life".² Medical humanities, like all other disciplines, is rooted in imaginative inquiry.

A dynamic communication between humanities, arts, and science can offer a challenge to medicine, as well as to the humanities. Developmental change is neither comfortable nor easy. Medical humanities, with the richness it has to offer practice as well as academic and intellectual pursuit and education, could support a rounded development of medicine, able to respond with cutting-edge research, as well as to human needs—social, ethical and scientific.

GB is involved in the first conference of the UK Association for the Medical Humanities, Durham University, July 21–22, 2003. I acknowledge the support of Brian Hurwitz.

Gillie Bolton

School of Humanities, King's College, London WC2R 2LS, UK
(e-mail: gillie.bolton@kcl.ac.uk)

- 1 Einstein A. Interview with Sylvester Viereck, 1929, Berlin. In: Taylor K. When fact and fantasy collide. *Times Higher Educational Supplement* Dec 20/27, 2002: viii.
- 2 Pattison S. Medical humanities: a vision and some cautionary notes. *J Med Ethics: Med Humanities* 2003; **29**: 33–36.
- 3 Downie RS. Medical humanities: a vision and some cautionary notes. *J Med Ethics: Med Humanities* 2003; **29**: 37–38.
- 4 Friedman L. The precarious position of the medical humanities in the undergraduate medical curriculum. *Acad Med* 2002; **77**: 320–22.
- 5 Evans M. The mind-body question. In: Louhiala P, Stenman S, eds. Philosophy meets medicine. Helsinki: Helsinki University Press/Signe och Ane Gyllenberg Foundation, 2000: 105–15.

- 6 Charon R, Montello M, eds. Stories matter: the role of narrative in medical ethics. New York: Routledge, 2002.
- 7 Carter MA, Robinson SS. A narrative approach to the clinical reasoning process in paediatric intensive care: the story of Matthew. *J Med Humanities* 2001; **22**: 173–94.
- 8 Brody H. Stories of sickness, 2nd edn. Oxford: Oxford University Press, 2003.
- 9 Council for Science and Technology. Imagination and understanding: a report on the arts and humanities in relation to science and technology. <http://www.cst.gov.uk/cst/imagination.htm> (accessed July 3, 2003).
- 10 Centre for Medical Humanities. The healing continuum: medical humanities and the good doctor. Conference in New York City, Oct 17–18, 2003: http://www.pcps.ucl.ac.uk/cmh/conference_2003.html (accessed July 3, 2003).
- 11 Evans HM, Greaves DA. Looking for emerging themes in medical humanities: some invitations to our readers. *J Med Ethics: Med Humanities* 2003; **29**: 1–2.
- 12 Calman K, Downie R. Why arts courses for medical curricula? *Lancet* 1996; **34**: 1499–00.

Ombudsman's seventh report

Four complaints were referred directly to the ombudsman in the past 12 months. One, relating to one individual's allocation of travel funds by *The Lancet*, fell outside the ombudsman's remit.¹ The other three cases are summarised in the panel.

Complaints July, 2002, to June, 2003

Case 1

Author of rejected letter alleged bias and possible lack of integrity on the part of the journal. No deficiencies identified in editorial process. Editorial decisions are not open to the ombudsman's scrutiny. Rejected.

Case 2

Delay of 17 months between receipt of manuscript and final editorial decision. Major defects found in editorial process consequent on prolonged absence of member of editorial staff through sickness and failure of manuscript-tracking system in the office. Failure partly mitigated by misdirection of some correspondence by authors and the journal's difficulty in finding appropriate external reviewers. Measures taken to ensure that similar gross failures do not occur again. Upheld.

Case 3

Delay of 4 months between submission of manuscript to *The Lancet Oncology* and editorial response, requesting revision. Revised manuscript rejected. Editorial processing confirmed to be slow, but problems encountered in finding external assessors prepared to review text. Initial editorial opinion eventually based on one external opinion and detailed inhouse assessment; judged to be sensible compromise. Subsequent editorial decision to reject revised version falls outside ombudsman's remit. Rejected.

The ombudsman's last report² noted *The Lancet's* protracted handling of letters responding to previous published papers. The editorial process has now been shortened.³

Richard Carter

c/o *The Lancet*, London NW1 7SY, UK

- 1 Horton R. *The Lancet's* ombudsman. *Lancet* 1996; **348**: 6.
- 2 Carter R. Ombudsman's sixth report. *Lancet* 2002; **360**: 272.
- 3 Mullan Z. *Lancet* correspondence: old letters, new rules. *Lancet* 2003; **361**: 12.