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News & Views

Profile: Professor John Mendelsohn

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Lessons learnt from Hurricane Ike last autumn are now guiding John Mendelsohn in his management of the largest US cancer institute in the current financial down turn. “We face critical financial pressures due to decreasing federal research support, cutbacks in Medicaid and Medicare, reduced philanthropic gifts, and increases in expenses for medically indigent patients,” says

Mendelsohn, president of the University of Texas M. D. Anderson Cancer Center. “We weathered the hurricane well, based on careful preparation and a spirit of dedication and teamwork when the storm arrived. It’s in the same spirit we’re planning to come through the adverse circumstances the nation now faces.”

Mendelsohn is a rare animal, a clinician who has excelled in multiple careers of scientist, author and administrative leader. The key to such success, Mendelsohn advises young colleagues starting out on their careers, is not to attempt to do everything at the same time. “As my research gained ground I cut back on clinical work, then as my administrative responsibilities became more demanding I closed my lab,” he says.

Mendelsohn was inspired to study molecular biology when he had the good fortune to be recruited to a research project in the laboratory of James Watson (of Watson and Crick/ double helix fame), while studying for his biochemistry bachelor’s degree at Harvard. “From Watson’s project on RNA metabolism I learnt how to do research in a critical and creative way, and was introduced to molecular biology, a field just starting to unfold,” says Mendelsohn, who went on to qualify in medicine and felt oncology provided the “best fit” with his research interests.

Undoubtedly Mendelsohn’s greatest contribution to research has been development of the targeted therapy cetuximab, known as Erbitux[®], with colleague Gordon Sato (who later took an entirely different tack and is now working on the world food crisis). The pair formulated their ground breaking hypothesis in 1980, while working at The University of California, San Diego that blocking the epidermal growth factor receptor (EGFR) would prevent cancer growth and reproduction by inhibiting the tyrosine kinase that is part of the receptor. Subsequently they proved their hypothesis by developing an anti-EGF monoclonal antibody that prevented the growth factor from docking to the receptor, thereby preventing receptor tyrosine kinase activation and inhibiting cancer cell growth. Mendelsohn and Sato demonstrated the effect in a cell culture in 1983 and in a mouse model in 1984. The FDA approved cetuximab for the treatment of advanced colorectal cancer in February 2004, and for head and neck cancer in March 2006. Today more than 130 clinical trials are underway using cetuximab to treat 15 types of cancer and two other diseases.

“We’re starting to appreciate tyrosine kinase inhibitors are unlikely to succeed in eliminating cancer cells on their own, and work best in combination with other drugs,” says Mendelsohn, adding that they are also finding abnormal pathways that bypass EGF, such as the K Ras mutation. “This is making the development of predictive markers vitally important to avoid treating the patients who are unlikely to respond.”

Other research highlights include conducting the first clinical trial showing that Herceptin used alone could produce a clinically useful response and in 2001 the first clinical trial demonstrating that the addition of an EGF receptor inhibitor could overcome resistance to a cisplatin in head and neck cancer.

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Mendelsohn's remarkable career trajectory has taken him from the University of California, San Diego, where he became an assistant professor of medicine in 1970, and later founding director of the university's Cancer centre in 1976 (at the tender age of 41), to the Memorial Sloan-Kettering Institute for Cancer Research, New York, where he was chairman of the Department of Medicine, and finally to MD Anderson where he was appointed president in 1996.

Mendelsohn feels the experience of running a research lab for over 20 years, together with his clinical career as a medical oncologist, treating all kinds of cancer, provided an ideal training ground for his current role heading MD Anderson. "At MD Anderson we've developed an integrated programme for cancer care, where doctors treating cancer are grouped into multidisciplinary teams by disease site, not by the type of doctor they are. The structure consists of teams of 10–40 people focusing on just one type of cancer. The fact I've treated patients from all these disease areas in the past means that although I no longer have the expertise to treat such patients I possess the knowledge to ask the questions that help me to decide priorities, says Mendelsohn, who feels he has an advantage over most university presidents who have to manage a far broader range of subjects from arts to the sciences.

Despite leading 17,000 employees, including more than 1400 faculty members, not to mention a volunteer corps of more than 1600 people, Mendelsohn still manages to maintain a "hands-on" style of management, continuing to teach students, playing an active part in fund raising, and a strategic role in planning the clinical research programme. In day to day activities he is enabled by the management organisation he introduced, with three executive vice presidents with separate responsibility for clinical activities, academic research and education, and business activities. "The structure frees me up to take an overview and provide strategic leadership, but I still like to get involved with the minutiae and enjoy having contact with patients when they come and ask me for advice," he says.

Mendelsohn continues to champion the concept of translational research, and has facilitated a clinical trial initiative at MD Anderson in lung and breast cancer involving prospective selection of appropriate targeted cancer treatments, based on real-time measurements of the patient's tumour biopsy of protein expression, gene mutation, copy number and expression. "Screens that normally take months need to be performed in 10 days in the programme to allow clinicians to select the most appropriate therapy. We're screening around half a dozen genes, and are also looking retrospectively at over 100 different genes. The price tag is substantial, with estimated costs of \$20,000 dollars for lab tests over and above treatment."

The concept, he says is simple. "We are gearing up to create a state of the art translational pathology laboratory which can expedite genetic and molecular assays on cancer biopsies that eventually will enable selection of optimal drug treatments for each patient," he says, adding that in future he hopes pharmaceutical companies will start to embrace this type of research, and realise that the approach will make their products more cost effective.

Under Mendelsohn's leadership M.D. Anderson has achieved top ranking four times in the past six years in the US News and World Report's "America's Best Hospitals". Other successes include M.D. Anderson ranking first in the number of grants awarded – including 10 Specialised Programs of Research Excellence (SPOR) grants and total amount of dollar grants from the National Cancer Institute.

"Until now we have been in a very strong growth mode, more than doubling in size in just about every parameter in the past decade," says Mendelsohn, who finds himself increasingly "challenged" by the economic situation and that more and more of his time is being taken up with prioritizing initiatives to match tightening resources.

Inspired by their successful management of Hurricane Ike, (where through extreme preparedness they were able to continue to provide acute care for all but 1.5 days), Mendelsohn has devised a financial warning system, to put the Centre on to different levels of financial stringency, ranging from level one, to the highest state of alert at level four. Finances are reviewed monthly, to allow "weather warnings", to enable them to "shift to a different level of preparedness".

"Currently we're on level one, which is all about doing the things you can to be efficient. The most drastic is level four, which means laying off personnel," he says, adding that this would be the last resort since such action would entail losing the skill base of a generation of scientists and causing hardship for many of our valued employees.

All is not doom and gloom, he feels sanguine that the new political administration will at last make a difference to health care. The zeitgeist, he maintains, is vastly different from previous attempts at health care reform. "There's enough pain now and concern that people are becoming prepared to compromise and to give a bit and not be so caught up in their vested interests," he says.

Other activities include publishing – he was the founding editor in chief of *Clinical Cancer Research* between 1994, and 2004, is on the editorial board of a number of journals (including *Molecular Oncology*) and edited three editions of "The Molecular Basis of Cancer". For relaxation he plays tennis, reads "fanatically" and visits eight grandchildren, ranging age from 1 to 14 years, distributed between the East coast and Europe. Together with his wife Anne – a former scientific film maker and early pioneer of distance learning, to whom he has been married for 47 years – he undertakes many civic duties in Houston. Keenly aware of the privilege of their own education, the couple are strong advocates for "Teach for America – Houston", a US scheme which recruits many of the nation's best and brightest young graduates to teach in public schools. Mrs Mendelsohn has served as chair of the Houston Regional board, and has been a member of the Presidents' Council of the national organisation. Mendelsohn is also active in an initiative to attract biotechnology companies to Houston. "It's important to MD Anderson, because good faculty like to be around biotech," he says.

Mendelsohn admits to envy of the next generation of oncologists who he believes stand a real chance of making an impact on the threat of cancer. "We'll never get rid of cancer

altogether, but better prevention, early detection, targeted therapies and improvements in chemo, radiotherapy and surgery should all radically decrease the burden,” he says. “Right now it’s just a wonderful field to be in.”

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