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This piece is a remembrance of Dr. John Mendelsohn, a towering leader in cancer medicine, on the occasion of his death anniversary on January 7. Amongst his many achievements, Dr. John Mendelsohn is recognized for targeting the first receptor tyrosine kinase (RTK) and developing the first anti-epidermal growth factor receptor (EGFR) blocking antibody as a cancer drug, Erbitux (Cetuximab), and revitalizing the field of targeted cancer therapeutics during the 1980s.1–3 In the decades that followed, Dr. Mendelsohn dedicated his career to helping patients by moving research discoveries from the bench to bedside and expanding access to care for cancer patients by building and/or uplifting three cancer centers.4–6

Today, targeted cancer therapy is considered a superior treatment option for human cancer. By its very definition, targeted therapy is designed to selectively impair the functionality of target molecule(s) or pathway(s), thereby minimizing nonspecific side effects of the drug. Over the years, such approaches have delayed the progression and recurrence of the disease in question, prolonging the lives of cancer patients, and at times, also curing some cancer sub-types, though infrequently. The field of targeted cancer therapy has undergone a major morphogenesis (and the process is ongoing) since the time Dr. Mendelsohn first hypothesized the notion of blocking the activation of EGFR by autocrine and/or paracrine growth factors using highly selective monoclonal antibodies, and consequently, interrupting the growth-promoting signals as an effective anticancer approach.1–3 As always, Dr. Mendelsohn pursued his hypothesis initially as an academic project but soon noticed a clear translational implication of his work. Although there was a growing recognition of widespread upregulation of hyperactivated EGFR in epithelial cancer, the notion of inhibiting EGFR – as an anticancer approach was new during the 1980s and viewed with some degree of skepticism until Dr. Mendelsohn and colleagues published their first set of landmark publications.7–10 Overtime, Mendelsohn’s blocking RTK hypothesis was readily followed by academic and pharmaceutical laboratories, in one form or another, and facilitated the development of a variety of therapeutic anticancer agents targeting the HER family of RTKs. Although Dr. Mendelsohn’s work primarily focused on EGFR11–15 and invented cetuximab,3 he and his colleagues also expanded the notion of blocking growth factor receptor antibodies to HER2.16–18 His team played a pivotal role in gathering proof-of-concept evidence of an anti-tumor activity of anti-HER2 mAb4D5, either alone or in combination with commonly used chemotherapeutics, and undertook early clinical trials of mAb4D517,18 which was later humanized and developed as trastuzumab (also known as Herceptin) by Genentech for breast cancer patients with HER2 overexpression.19 Lessons from anti-EGFR and -HER2 antibodies led the way for a wave of creative approaches to target the activation of RTKs at multiple layers by a variety of designer molecules beyond anti-receptor antibodies. In brief, Dr. Mendelsohn’s work on targeting the EGFR by blocking antibodies will always serve as a guidepost for our field of targeting RTK for therapeutic gains and represents one of the earliest advances in targeted cancer therapy.

Dr. Mendelsohn was an adventurer who took on new opportunities for scientific and research growth throughout his career. For example, while in the laboratory of James D. Watson at Harvard in early fifties he became fascinated with biochemistry and molecular biology, later traveling to the University of Glasgow as a Fulbright Scholar in Biochemistry. He always valued the importance of strong basic science in transforming translational research themes to the next level, a core principle by which he closely adhered to while developing therapeutic anti-EGFR antibodies as anticancer drugs. In addition, Dr. Mendelsohn always believed the significance of creating state-of-art infrastructure and platforms to nurture an outstanding scholarly culture to bring out the best of academic medicine in a hospital setting. For example, while in the early stage in his career, he championed the cause of creating the University of California at San Diego (UCSD) Cancer Center and served as a founding director from 1977 to 1985 before leading the Department of Medicine at Memorial Sloan Kettering Cancer Center (MSKCC). Likewise, as the President of The University of Texas MD Anderson Cancer Center (MDACC) from 1996 through 2011, he was responsible for revitalizing the institution to an unprecedented level, rebranding MDACC into a global institution and changing the benchmarks in all areas of cancer treatment as part of the mission of MDACC. Dr. Mendelsohn’s leadership style was personable, easy and friendly. These
humanistic traits became a powerful tool in his leadership, allowing him to not just build successful academic cancer centers, but also allowed Dr. Mendelsohn to raise philanthropic support to implement his causes.

In addition to his work building institutions and scientific advancement, Dr. Mendelsohn also played an active role in the mission of several professional organizations, especially the American Association of Cancer Research (AACR). He also had the honor of serving for over a decade as the founding Editor of Clinical Cancer Research – a flagship scientific journal from AACR. In fact, Dr Mendelsohn’s death anniversary coincides with the completion of 25 glorious years of the journal Clinical Cancer Research, which continues to push forward Dr. Mendelsohn’s legacy in high-quality clinical cancer research.

There are several other qualities of Dr Mendelsohn that stood out time and again over the course of his career, qualities that became assets and tools for his success. Dr. Mendelsohn always reached out to the best, even to those who might be viewed as competitors, and opening the way for novel collaborations and strengthened scientific discourse. He was an open book, sharing ideas and data fearlessly, seeking input from others, publically crediting those who deserved recognition, and always had enough time to maintain friendships and continue building relationships with new and old alike.

The field of Cancer Medicine will remain indebted to John Mendelsohn for pushing the frontiers in Targeted Cancer Therapy by making substantial advances to the biology of HERs and directly contributing to the development of two anticancer drugs, cetuximab and trastuzumab, medications that have benefitted cancer patients globally. Dr Mendelsohn’s work in the mid-eighties provided a much needed proof-of-concept behind a novel therapeutic approach. This work, targeting RTKs in human cancer, in-turn, catalyzed the timely development of RTK-directed targeted therapy as a whole and revolutionized the field. In closing, Dr. John Mendelsohn was a very special physician-scientist with a rare combination of scientific zeal, intellectual curiosity, dedication to his work, with the foresight to lead and develop a new treatment in cancer medicine. His scientific success was matched by his interpersonal charm, patience, humanity and respect for others that enveloped his leadership style. Dr. Mendelsohn’s professional career which spanned almost half a century has witnessed significant gains in cancer research and treatment. Surely, Dr. Mendelsohn will be missed by all in the cancer community, while his legacy will remain alive and continue to percolate the field of cancer biology and therapy through his work, his trainees and mentees, and cancer centers he built, strengthened or elevated in his long career.

References