MOORE'S LAW AND THE DEVELOPMENT OF BREAKTHROUGH BIOLOGICS

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The power of exponential growth can be wondrous, especially for a businessman like Ron Walker. The 76-year-old Australian is one of the country's wealthiest property developers and knows how compound interest affects investments. But Walker learned the hard way that the natural world is no stranger to rapid growth, and it's not always benign.

In healthy tissue, cell number doubles every division. But the same is true of cancer cells, a fact Walker discovered in 2012 when he was diagnosed with melanoma, the deadliest of skin cancers.[1]

Nine months later this aberrant doubling had led to tumors in his lungs, brain, bones, and adrenal glands. He was given a few months to live.

Standard treatment for melanoma includes surgery, chemotherapy, and radiation.[2] But now, thanks to advances in molecular biology, immunology, improved cell lines, transgenic mice, and product processing, it can also be treated with biologics: targeted therapies that hold great promise.

Walker first received an infusion of Yervoy (Bristol–Myers Squibb), which led to a severe autoimmune reaction that prevented further treatment. He then enlisted in a Phase 1 trial for Keytruda (Merck). He flew to Los Angeles, received his first infusion, went home, and waited.

There's a lot of talk these days in pharmaceutical engineering circles about Moore's Law, the famous observation that computing power doubles every two years. It turns out that many of the innovations that have benefited biopharmaceutical engineering have occurred at a similar pace.

After 2008, the cost of sequencing DNA dropped faster than Moore's Law, mostly because the process has become a billion times faster since the first genome was sequenced in 1977.[3]

Structural proteomics determines the three-dimensional structure of gene products and allows the rational design of novel drug compounds. The efficiency of X-ray crystallography has improved a thousand-fold since the 1960s,[4] meaning that the number of 3D protein structures available for analysis has grown from under 4,000 to over 112,000 in the past 20 years.

Combinatorial chemistry has led to libraries of lead compounds that are several orders of magnitude larger than those of the early 1980s.[5] High-throughput screening has contributed to a 10-fold reduction in cost compared to 1995,[6] while computer algorithms that screen libraries using target biomolecule data have sped up the pace of drug design.

As John Cox, an executive vice president at Biogen, has pointed out, the increase in active pharmaceutical ingredient product titers and the decreased price per gram of production have combined to improve production efficiency 200,000-fold.[7]

These exponential advances have helped big pharma's bottom line. Between 2008 and 2013, sales of full-length monoclonals produced in mammalian cells doubled,[8] while annual sales of the top-six-selling-biologics quadrupled between 2004 and 2012.

The obverse of these huge improvements in sales, efficiency, and reduced costs is the observation dubbed Eroom's Law: The number of new drugs brought to market per billion dollars of R&D declined two-fold every 9 years between 1950 and 2012.[4] Part of this is due to the 10- to 100-fold increase in the cost of bringing a new product to market since the mid-1980s.[9]

With a record number of drug approvals last year, the trend may have reversed, but it's too soon to tell.[10] Eroom's Law has been mitigated by the FDA fast-track process for breakthrough therapies, which can see a drug pass from Phase 1 trials to market in a year. In addition, the increasing costs of drug research and development are being recouped, in part, by exorbitant increases of drug prices.

Within 18 months of receiving his first infusion of Keytruda, Ron Walker was free of cancer. For a disease that is almost always fatal, these exponential improvements in the science and technology behind drug R&D provide patients like Walker the hope of a miraculous cure. ◂

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