**The growth of cell complexity**

This analysis from 20 years ago, when cells were classified by how they look, shows how cell type number rises as animals become more complex. Today, more cell types are recognized, making this curve even steeper.

---

**ONCOLOGY**

**Vitamin C could target some common cancers**

Therapy kills tumor cells with difficult-to-treat mutation

*By Jocelyn Kaiser*

Maybe Linus Pauling was onto something after all. Decades ago the Nobel Prize–winning chemist was relegated to the fringes of medicine after championing the idea that high doses of vitamin C could combat a host of illnesses, including cancer. Now, a study published online this week by *Science* reports that vitamin C can kill tumor cells that carry a common cancer-causing mutation and, in mice, can curb the growth of tumors with the mutation.

If the findings hold up in people, researchers may have found a way to treat a large swath of tumors that has lacked effective drugs. “This has the potential to be one answer to the question everybody’s striving for,” says molecular biologist Channing Der of the University of North Carolina, Chapel Hill, one of many researchers trying to target cancers with mutations in the so-called RAS gene family.

The failure of two clinical trials of vitamin C pills in cancer patients, conducted in the late 1970s and early 1980s at the Mayo Clinic in Rochester, Minnesota, dampened enthusiasm. Studies later suggested that the vitamin must be given intravenously to reach doses high enough to kill cancer cells, and a few small trials found hints that IV vitamin C treatment extended cancer survival when combined with chemotherapy. But doubters were not swayed. “The atmosphere was poisoned” by the earlier failures, says Mark Levine of the National Institute of Diabetes and Digestive and Kidney Diseases in Bethesda, Maryland, a collaborator on these trials.

In Baltimore, Maryland, found that large doses of vitamin C did indeed kill cultured cells with *BRAF* or *KRAS* mutations by raising free radical levels, which in turn inactivate an enzyme needed to metabolize glucose, depriving the cells of energy. Then they gave daily high dose injections—equivalent to a person eating 300 oranges—to mice engineered to develop *KRAS*-driven colon tumors. The mice developed fewer and smaller colon tumors compared with control mice.

Cantley’s lab and collaborators found that large doses of vitamin C did indeed kill cultured cells with *BRAF* or *KRAS* mutations by raising free radical levels, which in turn inactivate an enzyme needed to metabolize glucose, depriving the cells of energy. Then they gave daily high dose injections—equivalent to a person eating 300 oranges—to mice engineered to develop *KRAS*-driven colon tumors. The mice developed fewer and smaller colon tumors compared with control mice.

Cantley hopes to soon start clinical trials that will select cancer patients based on *KRAS* or *BRAF* mutations and possibly GLUT1 status. Bert Vogelstein of JHU, in whose lab Yun noticed the GLUT1 connection, is excited about vitamin C therapy as well, not only as a possible treatment for *KRAS*-mutated colon tumors, which make up about 40% of this cancer type, but also for pancreatic cancer, a typically lethal cancer driven by *KRAS*. “No *KRAS*-targeted therapeutics have emerged despite decades of effort,” Vogelstein says.

Others are intrigued but caution that the effects seen in mice may not hold up in humans. Still, because high dose vitamin C is already known to be safe, says cancer researcher Vuk Stambolic of the University of Toronto in Canada, oncologists “can quickly move forward in the clinic.”