

## For cancer, timing and order of mutations determine outcome

For the first time, researchers have proved that the order in which cancer genes mutate affects the type of malignancy that results and its response to treatment. Although the findings are specific to a particular group of preleukemic disorders known as myeloproliferative neoplasms, they suggest that scientists studying other types of tumors should start taking into account the timing of the underlying genetic mutations as a potentially critical factor in establishing an accurate diagnosis as well as in making choices about treatment.

The study, which was conducted by investigators in the U.K., Spain and Germany, was published in the [February 11 issue](#) of *New England Journal of Medicine*.

Myeloproliferative neoplasms are particularly compelling cancers to study, from a scientific point of view, for two reasons: as disorders of the blood, their cells are very easy to sample via routine blood tests; they represent the earliest stages of cancer growth, so it is easier to determine the order in which the genes in its cells mutated.

Two of the most important genes in the development of myeloproliferative neoplasms, previous studies have shown, are called *JAK2*. *TET2* is a tumor suppressor gene—so when it becomes defective, it's like disabling the brakes on a runaway car. *JAK2* amplifies the effect of growth signals in a cell. So when it gets stuck in the “on” position, it's like pressing on the accelerator of a runaway car. The researchers determined that patients in whom the *JAK2* gene had undergone mutation before the *TET2* gene were more likely to suffer blood clots, among other maladies, than their *TET2* -first counterparts, but their cells were more sensitive to anti-*JAK2* drugs.

A follow-up study showed that *JAK2* -first patients also tended to develop the disease at a younger age (in their late 50s and early 60s rather than about 10 years later). That doesn't necessarily mean that having *TET2* mutate first was any better as that mutation is known to predispose people to developing full-fledged leukemia.

**Read full, original article:** [Mutation Order in Tumor Genes Affects Cancer Outcomes](#)