In the 1970s, an assay was developed by Dr. Bruce Ames [1] that revolutionized the ability to test if a compound causes cancer or not.

Since then, the Ames test has been used on everything from food dyes to pesticides. The power of the Ames test is not only that it is incredibly efficacious, but also that it is inexpensive and relatively easy to do.

The test is based on a brilliant observation made by Dr. Ames. He realized that there is a strong linkage between the ability to cause mutations in DNA and the ability to cause cancer. To simplify what is an incredibly complicated process, the more mutations that something creates (or, the more mutagenic it is) the more likely it is to cause cancer. Fewer mutations = less cancerous.

In order to understand whether or not something causes cancer, you have to understand how the Ames test works.

The assay takes advantage of certain strains of bacteria (Salmonella typhimurium) that have been altered in multiple ways that make them well suited to be used in this test. For example, they have been made "leaky" so that the compounds being tested can enter into the bacterial cells.

But, the key reason that these bacteria are so useful - stay with me here - is due to their inability to make an essential amino acid - histidine - which is required for survival. If bacteria (or any living organism) cannot make histidine, they cannot survive. The reason why these strains of Salmonella typhimurium, referred to as His-, cannot make histidine is because they have a mutation in the genes that are responsible for histidine production.

Now for the assay....

When these His- strains of Salmonella typhimurium are exposed to a compound that induces
mutations in DNA, mutations will occur all over the DNA, in many genes. When some of those
mutations land in the genes that are responsible for histidine production, a number of bacteria will
regain the ability to make histidine. So, the Ames test uses a His- mutant strain to be able to
measure how many of those bacteria revert back to being able to make histidine again.

These reverted strains can be seen by growing the bacteria on agar plates lacking Histidine. In this
case, only those bacteria that can make their own histidine are able to grow to form a bacterial
colony, as shown in the photo above.

And, here is where we get information about cancer.

The more bacteria that are able to make histidine - the more mutations were made - the more
cancer that compound will likely cause.

Another truly brilliant realization by Dr. Ames makes the assay even more predictive. Sometimes
the chemical to be tested will not create mutations, but still be a cause for concern. This is
because, although the chemical itself is not carcinogenic, it can be metabolized to something that
is. Because the liver is the primary source of metabolism Dr. Ames addressed this problem by
adding extracts of rat livers to the assay. Rat liver extracts are known to be effective at
metabolizing chemicals, so the Ames test can not only test a chemical, but also, what it is
expected to become in a human body.

Lastly, different strains of *Salmonella typhimurium* are used in the Ames assay. What is the
difference between them? Although they all have mutations that make them unable to make
histidine, they vary in the types of mutations that they have. In using more than one type of
mutation, the assay can give more detailed information as to the type of mutation that the
compound causes. Does the compound, for example, change one DNA base pair? Or, does it
remove a base? Or add a base? The more His- strains that are used, the more information can be
gleaned from the assay.

The Ames test has been in use for over 40 years, and continues to be useful today. In searching
Pubmed, there are articles published within the last month or two with "Ames test" in the title
including,

- Lanthanum nitrate genotoxicity evaluation: *Ames test*, mouse micronucleus assay, and
  chromosome aberration test [2]. Mutat Res. 2016 Nov 1;810:1-5.
- A knowledge-based expert rule system for predicting mutagenicity (*Ames test*) of aromatic
- Genotoxicity assessment of low-level doses of gamma radiation with the SOS chromotest

The Ames test will certainly be used for years to come, aiding greatly in the enormous task of
deciphering what on this earth has the ability to cause cancer.

Links