



UNIVERSITY OF HAWAII
CANCER CENTER

What discovery is described in the Nature article?

Dr. Michele Carbone and his colleagues discovered why some people are more susceptible than others to asbestos, radiation, UV-light and other environmental carcinogens.

Although many people are exposed to asbestos, Ultraviolet light, radiation, etc., only a fraction of them gets cancer. We did not know why. Carbone and colleagues discovered that a gene called BAP1 regulates a channel inside the cell called IP3R3 that moves Calcium. When the BAP1 gene is mutated (some people are born with a mutated BAP1 gene) or damaged in tumor cells (this gene is damaged in most cancers, so it does not work), Calcium levels inside the cells decrease. The decrease of Calcium makes cells much more likely to become malignant when exposed to carcinogens such as radiation, Ultraviolet light or asbestos.

If cells are already malignant (*i.e.*, if these are tumor cells), when BAP1 is damaged they become resistant to chemotherapy. The tumor cells of over 70% of mesotheliomas—the cancer often caused by asbestos—90% of eye melanomas, renal cell carcinomas, and many other cancers have mutated BAP1 and thus are more resistant to chemotherapy.

Why is it important?

You cannot fix something unless you know what is broken. Now we know exactly what is broken: this BAP1-regulated Calcium channel. Carbone's team is already working at fixing this Calcium channel; when they fix it, they should be able to prevent cancer in people who have inherited BAP1 mutations and to treat cancers whose tumor cells have developed BAP1 mutations.

About 20% of all cancers have BAP1 mutations, and these are the most aggressive cancers because they are resistant to chemotherapy. Carbone hopes that by fixing these Calcium channels, they will make these cancers much more susceptible to therapy.

Can you tell me more information about BAP1 mutations?

In 2011, Carbone and colleagues discovered “the BAP1 cancer syndrome” uncovering why certain families had a high incidence of mesothelioma (the cancer caused by asbestos), melanoma and other cancers (Carbone *et al*, Nature Genetics, [Germline BAP1 Mutations predispose to malignant mesothelioma](#), 28 August 2011, DOI 10.1038/ng.912).

Since Carbone's team published their paper in 2011, there have been over 450 publications on BAP1, 417 of which cited the 2011 paper (6/1/17).

Now the Carbone team has figured out exactly how the BAP1 gene works. The publication of this current paper in *Nature* shows the power of collaboration and the fact that (thanks to technology) we can overcome Hawaii's geographical isolation and turn it to our advantage, making Honolulu the place where scientists from Asia, Europe and mainland USA meet to work together to find new ways to fight cancer. For example, several scientists from Japan, Italy, China, and the US mainland come regularly to work in Carbone's lab at UHCC for several months each year. These scientists are among the best in the world, and include a Nobel Prize winner, Bruce Beutler, members of the US National Academy of Sciences, etc.

Does Dr. Carbone work with patients?

Patients from all over the world also come to be studied by Carbone's team, which works with them *pro bono*. These patients become friends with Carbone and with his team, and they are in this fight to find a cure together.

What are you looking forward to potentially discovering through this research?

I want to prevent and cure cancer in as many people as possible. We have been fortunate to see that our research and discoveries have already led to preventive measures that are expected to save many lives in the coming years.

Now I want to develop a new therapy to help those who have cancer. I hope we will have the data to start a clinical trial to restore the normal activity of this IP3R3 Calcium channel within the next five years. We are already planning this trial with my collaborator [Dr. Harvey Pass](#), director of Thoracic Surgery at New York University. Hopefully, this trial will show that by fixing this BAP1-regulated Calcium channel we can save lives.