Scientists devise method for rescuing genetic material from formaldehyde-treated tissue samples

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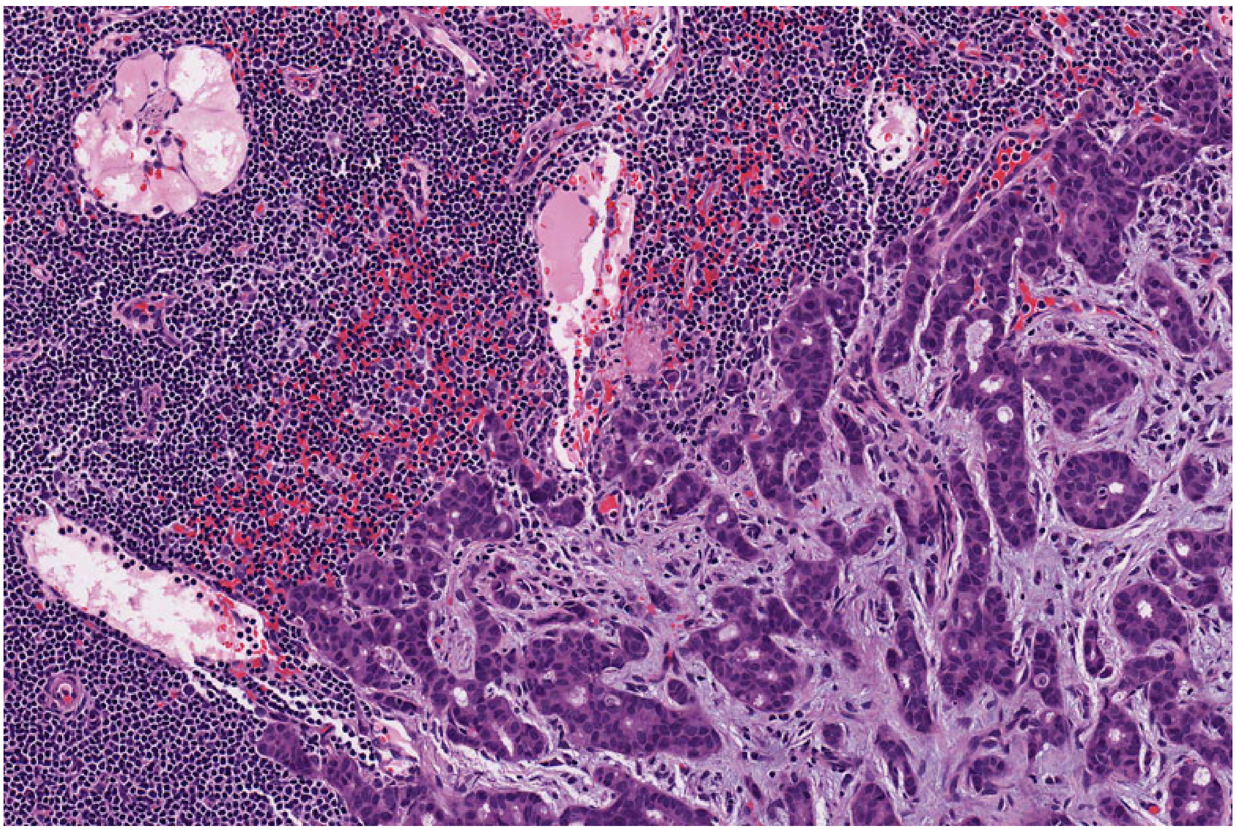

A new, catalyst-driven technique could free genetic material from formaldehyde-preserved cancer cells, like those pictured here, and lead to better personalized cancer treatments.

Each year, millions of tissue samples are collected from cancer patients and preserved in formaldehyde. The chemical "freezes" the cancer cells within the sample, allowing physicians to look at the disease and plan a specific course of treatment.

The process, however, coats the genetic material within the tissue, making it difficult to apply next-generation genetic analysis that could reveal better, personalized therapies. Now, a team of Stanford chemists and physicians has developed a technique that significantly improves the recovery of genetic material from those samples.

"Pathologists used to just look at tissues under a microscope, so it didn't matter that formaldehyde was there," said Eric Kool, a professor of chemistry at Stanford and senior author on the study. "The trend now is to treat people based on their genetic situation, and the problem is, the formaldehyde gets in the way of this. We've found a way to reverse the process."

Scientists and physicians are eager to know both the quantity and sequence of RNA – the genetic material responsible for coding proteins – within a tissue sample, as this information can greatly improve the diagnosis of the disease. This in turn can inform the best route of treatment and lead to better and more accurate prognoses. For instance, one genetic variation of a particular type of cancer might respond well to a specific drug therapy, while another fares better with radiation.

When the formaldehyde "fixes" the tissue, it bonds tightly to the RNA. The most effective means of removing the formaldehyde, however, involves heating the sample, which has undesirable effects.

"Heat destroys RNA faster than it removes formaldehyde," Kool said. "What little we can recover from the sample is difficult to read."

Kool and his colleagues specialize in RNA and DNA chemistry, and they developed catalyst molecules that could operate at mild temperatures to selectively break the bonds between the formaldehyde and RNA, leaving the genetic material free and undamaged. The approach, Kool said, could conceivably be used to process any tissue sample.

Formaldehyde presents the same challenges with rescuing DNA and proteins from samples, so Kool and his colleagues are now investigating whether a similar catalyst-based approach could improve the recovery of those molecules as well.

The study is published in *Nature Chemistry*, and was co-authored by Ash Alizadeh, Luzi Barandun, Thomas Ehrenschwender, Emily Harcourt, David Hewings, Saswata Karmakar, David Kurtz, Alexander Lovejoy and Caroline Roost. A company, Cell Data Sciences, has been founded to develop and commercialize the technique.

More information: "Organocatalytic removal of formaldehyde adducts from RNA and DNA bases." *Nature Chemistry* (2015) DOI: 10.1038/nchem.2307

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