Just like Wolverine, humans need metal to maintain strong bones

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Credit: University of Manchester

An international team of researchers, led by The University of Manchester, has used the UK's Diamond Light Source facility (pictured above) to image the precise location and chemistry behind the growth in bone for the first time. Their research has provided fresh insight into how bones grow and develop, and how the traces of metal found in bones play a vital part in this process.

The team analysed how mammal bones grow by studying the skeleton growth of rodents – and how this process links the common man and fictional superhero Logan.

Unlike Wolverine from the X-Men, mammals do not obviously sport metal claws. However, all vertebrates, including mammals rely on tiny concentrations of trace metal in our bones to control their formation, growth and repair.

Wolverine's skeleton is made out of the fictional alloy adamantium, whereas the trace metals found in human bones include copper, calcium, zinc and strontium.

"The reason bone needs to be able to store these metals is that many biological processes rely on the tiniest traces of chemical elements like zinc and strontium," said Dr Jennifer Anné. "A good example of that is what we are seeing in the developing skeleton of our mouse."

The process responsible for the development of most of the bones in the body (endochondral ossification) is layered into distinct areas of activity from the centre of the developing bone to its extremities. These areas can be simplistically placed into three categories: cartilage, replacement and mineralised (ossified) bone.

A seemingly straightforward three-step process, from soft cartilage to mineralised bone, is actually a complex cocktail of growth hormones and proteins that few fully understand. Luckily, these processes get a little help from the periodic table that leaves elemental fingerprints that have now been identified and read by the team.

Lead author Dr Jennifer Anné explains how studying these fingerprints will tell us more about how bones are formed: "We found that the different steps that occur as the skeleton goes from cartilage to bone were highlighted in the corresponding element needed for this processes to occur. You get to see a snapshot of these processes occurring throughout the limb; something that hasn't been imaged before."

Although it is well known that certain metals can aid in bone health, this is the first time that these metal helpers have been imaged spatially as they weave their bony scaffold. Intensely bright X-rays generated by Diamond allowed the team to produce detailed images of where these minute metals were located within the tiny bones of the mouse limb.

Co-author Dr Nicholas Edwards from The University of Manchester said: "We focus on the trace elements rather than the proteins themselves because of the preservation potential of the metals, which means we can image biological processes from the recent to the ancient."

This is not the only time the team has used this X-ray light, which is 10 billion times brighter than that of the Sun, to visualise the chemistry in bone. Their previous work has looked at the beautiful preservation of biochemistry in fossil organisms, in birds, dinosaurs, manatees and plants up to 150 million years old. The results from this work highlight not only the importance of synchrotron-based imaging but hint at the possibilities to come.

Professor Fred Mosselmans, Science Leader on the I18 beamline at Diamond, said: "We're proud to support a wide portfolio of bone research across a number of our beamlines, and this is another good example of how we're supporting interdisciplinary research at Diamond. I18 allows researchers to detect and quantify elements using a tiny beam of X-rays. The technique is incredibly sensitive, so where elements are present in minute concentrations, our beamline is still able to detect them. This is useful in material science, chemistry, environmental science, as well as biology."

The research group will be scanning some new fossil material at the Stanford Synchrotron Radiation Lightsource in California this spring. The research on the mouse will be used to help the team identify ossification and other bone processes such as remodelling and cartilage replacement in the fossil record, from fossil mice to dinosaurs.

More information: Jennifer Anné et al. Visualisation of developmental ossification using trace element mapping, *J. Anal. At. Spectrom.* (2017). DOI: 10.1039/C7JA00042A

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