Healthcare industry BW

# The kidneys – underrated organs

**It was pure coincidence that Florian Lang chose the kidneys as his research object. Today, the physiologist from Tübingen is one of the most cited German kidney and hypertension specialists. Lang, who is 70 this year, mainly works with the regulation of ion channels and transporters in renal and other cells.**

"Many people just see the kidneys as excretory organs," says Lang. "They usually overlook the fact that the kidneys and their complex feedback loops affect the whole body." For the past 40 years, Lang, who is a professor at the University of Tübingen, has, amongst other things, been studying the body's phosphate levels, which are regulated by the kidneys.

When the kidneys fail, they can no longer effectively excrete phosphate and other substances with urine, and the blood phosphate level increases massively. Higher than normal phosphate levels in turn stimulate differentiated tissue cells to turn into bone- and cartilage-like cells and excrete the calcium phosphate mineral hydroxyapatite. What normally gives bones their strength is fatal for blood vessels. They calcify and increase the risk of dying from cardiac infarction or stroke.

Florian Lang has been an active researcher for over 40 years.
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## A fountain of youth for the sick and elderly

Lang's team has only recently discovered in a mouse model that ammonium chloride is able to interfere with the phosphate-induced reprogramming of the cells, resulting in a reduced deposition of calcium in tissue. Treatment improved the survival of the mice which then lived to the age of 1 or two years instead of only three months. This is more or less the normal age of healthy mice. "A spectacular result," says Lang, with obvious enthusiasm.

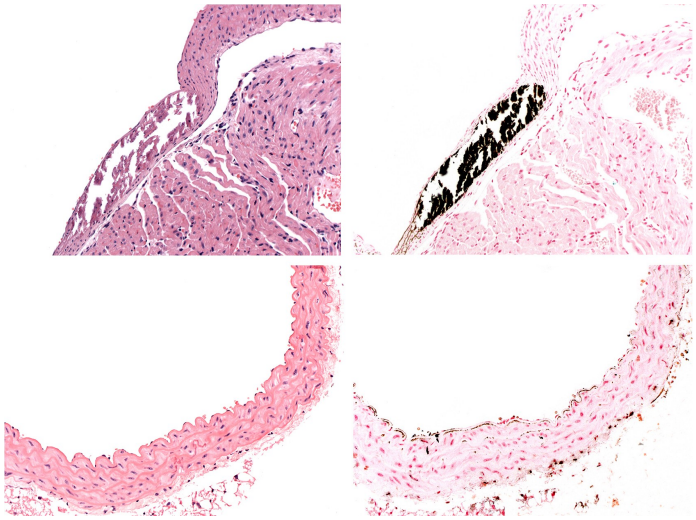
This discovery by the Tübingen researchers might be beneficial for patients other than those with kidney diseases. "In mice, calcification of blood vessels leads to a broad range of age-associated diseases such as cognitive impairments, thin skin and muscle loss," explains Lang. "Calcification is a typical sign of old age, and also occurs in people who do not have kidney problems. It is assumed that calcification contributes considerably to the development of age-associated diseases," Lang says.

## Two sides of the coin

Although Lang's research seems repeatedly to lead him away from the kidneys, he always comes back to this unique organ. In 1997, Siegfried Waldegger, a member of Lang's team, discovered SGK1, an enzyme that activates certain ion channels and transporters in cells, thus ensuring cell survival. "People exposed to high temperatures in deserts need the enzyme to protect their cells from dehydration. Marathon runners need the enzyme to prevent the blood circulation from collapsing," says Lang. In the Stone Age, the enzyme was crucial for survival as it initiated the 'fight and flight' response in the presence of wild animals. It reduces the amount of salt excreted, which causes a steep rise in blood pressure.

In modern humans, activation of the enzyme is associated with hypertension, obesity and diabetes, amongst other things. The enzyme is also thought to be responsible for the resistance of tumours to therapy as well as fertility problems. Drug producer Merck, with Lang's support, has developed a substance that blocks the enzyme. Perhaps it will one day be used to treat obesity or hypertension, or to break the resistance of tumour cells to therapy.

## Red blood cells commit suicide



Histological preparations of murine blood vessels stained with two different methods (left and right). Top: Blood vessels with calcifications (top). Bottom: No calcification due to mice having been treated with ammonium chloride (bottom).


Florian Lang has spent a great deal of time identifying the ion channels that cause the cells that undergo programmed death to shrink. Erich Gulbins from Lang's research group discovered that the death of a host cell is needed in order to position the immune defence against invading pathogens. Red blood cells, which lack a nucleus, can also commit suicide. Lang's research group was one of the first to demonstrate this. The suicidal death of erythrocytes is called eryptosis and has been shown to be associated with a number of diseases as well as triggering anaemia.

"It used to be commonly believed that patients with renal insufficiency and the elderly formed fewer erythrocytes. However, that's only half the truth. Erythrocytes die prematurely in the elderly and in people with renal insufficiency," says Lang. And so it appears again.... ageing is a topic that seems to attract the scientist who is nearly 70 years old himself. Coincidence? "I don't do this type of research for myself," says Lang. Nevertheless, he might find the eryptosis inhibitors developed by his research group helpful at some stage in his own life.

Lang has no plans to retire, although retirement would be well-deserved. "Research is great fun and as long as young scientists still ask me for advice, there is no reason for me to quit," says Lang. "I have great staff and an excellent research environment at the University of Tübingen," he adds. He has no regrets about swapping his doctor's coat for a lab coat. "I can save more lives with a research breakthrough than I would ever have been able to do as a doctor," says Lang. His four children have inherited his scientific curiosity. Like their father and grandfather, they have all studied medicine and taken their first steps in the laboratory under their father's wing.