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New cause of high blood pressure and heart disease discovered

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Why phosphate rich foods can increase blood pressure and promote vascular calcifications has been discovered by scientists at the Vetmeduni Vienna. The key is the hormone, FGF23—Fibroblast Growth Factor 23. When the level of FGF23 is raised, as through a high phosphate diet, calcium and sodium accumulate, putting strain on the cardiovascular system. The study appears today in the journal, *EMBO Molecular Medicine*.

Phosphate rich foods include processed cheese, Parmesan, cola, baking powder and most processed foods. Phosphates are widely used in the food industry as preservatives and pH stabilizers. When large quantities of phosphates are consumed, production of the FGF23 hormone is stimulated, which has a negative effect on the cardiovascular system. Reinhold Erben, the head of the Unit of Physiology, Pathophysiology and Biophysics at the Vetmeduni Vienna, warns that "our phosphate consumption is relevant for our state of health."

Over 500 million people around the world suffer from chronic kidney disease. Clinical studies have shown that these patients often develop cardiovascular diseases such as high blood pressure and vascular calcification. Until now, the connection between renal disease, the accumulation of the hormone FGF23 which is produced in the bones, and cardiovascular disease was unclear.

FGF23 controls renal excretion of sodium, and so the

blood pressure

The researchers showed that FGF23 has a so called sodium conserving effect, meaning it controls the reabsorption of filtered sodium in the kidneys. Mice lacking FGF23 excrete higher amounts of sodium in their urine, resulting in low blood pressure. Animals with high FGF23 levels show high levels of sodium in their blood, and in turn, high blood pressure.

A raised level of FGF23 puts increased strain on the heart. Reinhold Erben explains that, "In patients with chronic renal disease, both the phosphate levels and the levels of FGF23 are chronically high. This often leads to cardiovascular disease.

FGF23 controls calcium, and therefore vascular calcification

A second study, published by Erben's group in mid-January in *EMBO*, showed that FGF23 also controls calcium levels. As with sodium, the calcium is filtered in the kidneys and reabsorbed back into the body. If this reabsorption does not take place, the body loses calcium. Too much FGF23 leads to increased take up of calcium by the kidneys, and results in vascular calcification. Olena Andrukhova, the leading author of both studies, is keen to stress that, "Patients with chronic kidney disease often also suffer from cardiovascular disease. Raised FGF23 levels are partly responsible for this. Our results for the first time are able to explain this connection."

Feedback loop between kidneys and bones

The hormone FGF23 is formed in the bones and controls the excretion of phosphate via the kidneys. When there is too much phosphate present

in the body, the FGF23 level rises which leads to the excretion of excess phosphate. If too much phosphate is ingested with food, or if the excretion process via the kidneys does not work correctly, phosphate and FGF23 levels increase. A dangerous spiral begins that can have serious consequences on the overall health.

New critical values of FGF23 in science

The newly discovered functions of the hormone FGF23 were, until recently, attributed to another protein, αKlotho. Several scientific publications had assumed αKlotho to be the crucial factor for calcium conservation in the kidneys. With their newly published work, Erben and his colleagues show for the first time that FGF23 is responsible for this function, and not αKlotho. However, αKlotho is essential for the FGF23 effects, because it acts as a co-receptor for FGF23. Andrukhova stresses that "The focus in science is increasingly shifting from αKlotho to FGF23. The level of FGF23 in kidney patients can even indicate their life expectancy. The inhibition of FGF23 or its pathway could be a possibility to bring cardiovascular disease and vascular calcification under control."

More information: The article "FGF23 Regulates Renal Sodium Handling and Blood Pressure" by Olena Andrukhova, Svetlana Slavic, Alina Smorodchenko, Ute Zeitz, Victoria Shalhoub, Beate Lanske, Elena E. Pohl and Reinhold G. Erben will be published today in the Journal *EMBO Molecular Medicine*. DOI: 10.1002/emmm.201303716 embomolmed.embopress.org/cgi/doi/10.1002/emmm.201303716

The article "FGF23 promotes renal calcium reabsorption through the TRPV5 channel" by Olena Andrukhova, Alina Smorodchenko, Monika Egerbacher, Carmen Streicher, Ute Zeitz, Regina Goetz, Victoria Shalhoub, Moosa Mohammadi, Elena E. Pohl, Beate Lanske and Reinhold G. Erben was published on the 17th of January 2014 in the

Journal *EMBO*. DOI: 10.1002/embj.201284188
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