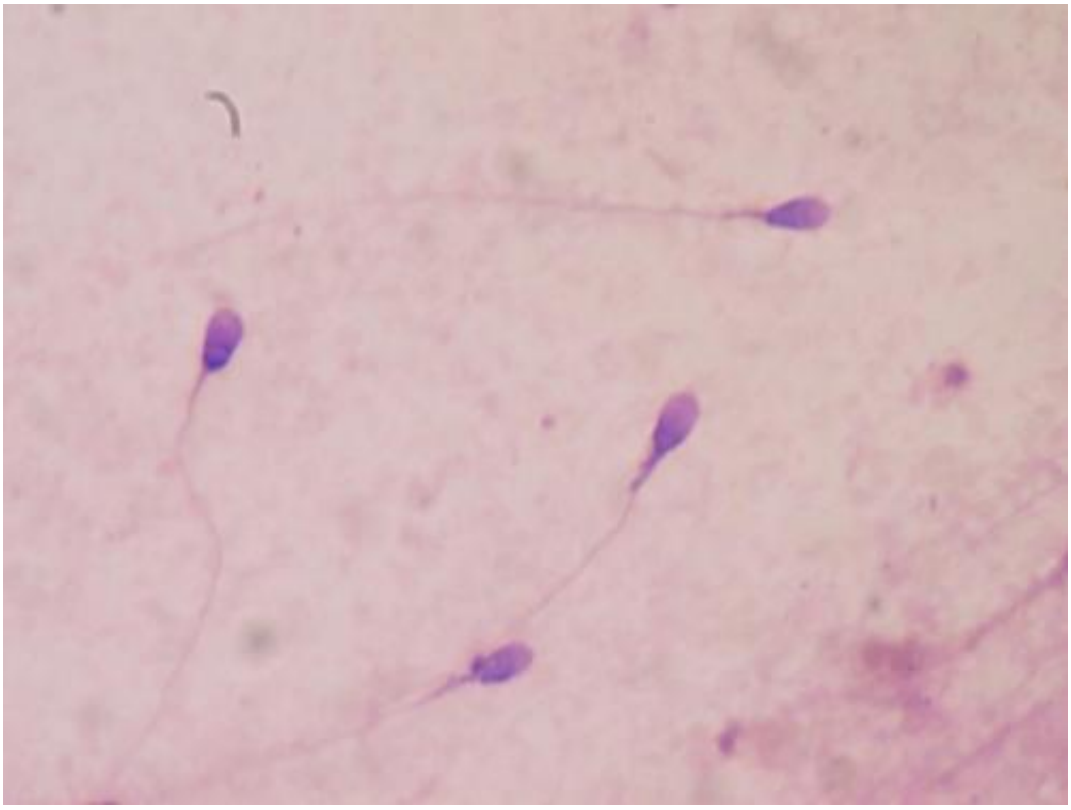
Researchers identify unexpected functions in the determination of height for a gene expressed in sperm

May 28 2015, by Anne Dreyfuss



Human sperm stained for semen quality testing in the clinical laboratory. Credit: Bobjgalindo/Wikipedia

An interdisciplinary research team led by the deans of Virginia Commonwealth University's Schools of Medicine and Engineering has

for the first time explained the association between human height and a specific protein-coding gene that is found in sperm.

Although the sperm associated antigen 17 (SPAG17) gene has been linked to human height in previous studies, it was not clear how the gene influences linear growth and skeletal development until now. VCU researchers found that a targeted mutation in the gene leads to skeletal malformations in mice, such as a shortened hind limb length, fused segments of the sternum and defects in bone mineralization.

Humans have the SPAG17 gene and genetic variants in that gene are associated with stature. "The mouse tells us the relationship between SPAG17 and bone length, which would explain why there is an association with height," said Jerome F. Strauss III, M.D., Ph.D., dean of the VCU School of Medicine.

Strauss is a professor in the Department of Obstetrics and Gynecology and researchers in his lab encountered the SPAG17 gene while they were investigating genes that affect male infertility. SPAG17 is one of the genes that controls sperm motility, so the researchers created a mouse that does not produce SPAG17, expecting to find a phenotype that exhibited male infertility.

"It turned out that this animal had other defects that we hadn't anticipated," said Maria Teves, Ph.D., who is a postdoctorate researcher in Strauss' lab and was the first author in a study titled "SPAG17 Deficiency Results in Skeletal Malformations and Bone Abnormalities," which will be published in *PLOS ONE* journal at 2 p.m. on May 27. "The animals died within 12 hours of birth, their tibia and femur were shorter than the wild-type mice, and they had skeletal malformations and bone mineralization defects."

That was when Strauss enlisted help from Barbara D. Boyan, Ph.D., dean

of the VCU School of Engineering. Boyan specializes in musculoskeletal biology.

"Researchers from Strauss' lab could see that a problem had occurred, but there are many techniques that we use in biomedical engineering that let us narrow in on what the defect is," Boyan said.

Researchers at her lab analyzed the shapes of the bones and the way they developed in the embryos. They also did cell culture studies in which they isolated cells from the defective animals to see if the defect in limb length was due to a fundamental alteration in their ability to form bone.

Ultimately, researchers from labs at both schools concluded that the bone malformations in the mice were due to the targeted mutation of the SPAG17 gene and that bone-forming cells also express this gene.

"This was an unexpected finding," Boyan said. "It is not a protein that anybody in my field would have thought to look at."

Researchers emphasize that more studies are needed to fully understand how SPAG17 affects bone and bone structure.

"Our findings are very important because they have revealed functions for SPAG17 that extend the role of this gene to regulation of skeletal development, growth and mineralization," Teves said. "This was just the beginning. The next step is trying to find the mechanisms of why this gene influences skeletal development."

More information: "Spag17 Deficiency Results in Skeletal Malformations and Bone Abnormalities." *PLoS ONE* 10(5): e0125936. DOI: 10.1371/journal.pone.0125936