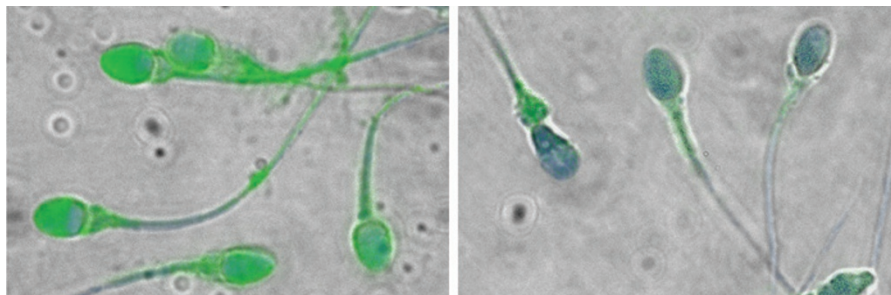


## MALE FACTOR INFERTILITY

## Mutation of sperm defensin causes subfertility

Despite improved methods for evaluation of sperm quality, infertility (defined by WHO as the inability to conceive after 1 year of unprotected intercourse) remains unexplained in about 20% of affected couples. Gary Cherr and colleagues now report that a common deletion variant—denoted '*del*'—in the gene encoding beta defensin 126 (DEFB126) could have a role in male factor infertility. “Our [study] shows that men with the *del/del* genotype are significantly less fertile than men who carry the wild-type allele,” they write in their *Science Translational Medicine* paper.

DEFB126 is a glycosylated polypeptide that coats the plasma membrane of sperm and provides protection against the female immune system. It thereby helps sperm move through the cervical mucus and attach to the fallopian tube. The authors demonstrate that the *del* variant is found in about 50% of alleles in general population cohorts from Asia, Europe, and Africa. Moreover, sperm from men with the *del/del* genotype had reduced surface



Sperm from donors with *wt/wt* genotype (left) and *del/del* genotype (right) labeled with fluorescent lectin specific for O-linked carbohydrate (green). *del/del* sperm have reduced surface glycosylation. Courtesy of G. Cherr.

glycosylation (see image) and difficulty penetrating surrogate cervical mucus *in vitro*. Surprisingly, lack of *DEFB126* did not affect sperm velocity or morphology.

Next, the researchers randomly selected 509 young couples in China with no history of infertility who were attempting unassisted conception. During follow-up (median duration 22 months) the wives of men harboring the *del/del* genotype were 12% less likely to have become pregnant and to have had a live birth compared with the spouses of men who had the

*wt/del* or *wt/wt* genotypes. “*DEFB126* genotype could be a useful parameter in evaluation of male infertility,” the authors assert. “By establishing genotype early ... clinicians could justify rapid progression to directed interventions [such as assisted reproduction].”

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