Female gametes prefer sperm with different immune genes

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Male stickleback displaying courtship colours. In this species, the females carefully choose their mating partners. However, they can never be sure that their offspring receive the optimal combination of immune genes. Therefore, the females' egg cells have found a way to select sperms with matching immune genes. Credit: MPI f. Evolutionary Biology/ M. Schwarz

Through clever partner selection, animals can increase the future success of their offspring. With some species, this process continues even after the sex act. Researchers at the Max Planck Institute for Evolutionary Biology in Plön have discovered that among sticklebacks, the egg cells of the fish are involved in the decision regarding fertilisation. An

accumulation of genes in the genetic material of the male gamete's cells determines which sperm is allowed in to the egg cell. Since vertebrates are highly similar in terms of their immune system, including with regard to the gene complex in question, the researchers assume that egg cells of other vertebrates – perhaps even those of humans – are able to control their fertilisation.

It is not only the obvious properties of an organism, such as size, speed or strength, that always decide whether an individual will survive. Without a powerful immune system, no animal can survive for long, let alone produce offspring. Since half of the immune genes of both parents respectively are passed on in combination to the offspring, it is worth selecting a sex partner who best supplements one's own immune genes.

But how can a partner with the right immune system be identified? Many vertebrates can smell the body's own defence mechanism of members of the same species. Even humans have this ability. At the University of Berne, Manfred Milinski, who later conducted research at the Max Planck Institute for Evolutionary Biology in Plön, discovered several years ago that women find the smell of men more attractive whose immune system supplements their own to the best possible degree.

Here, a decisive role is played by the genes of the "Major Histocompatibility Complex (MHC)", an accumulation of extremely variable immune genes on chromosome 6. "We already discovered some time ago how the gene complex impacts the smell of a human body, and identified our body's own perfume. This plays an important role when we select a partner," Milinski explains. "With such immune genes, which complement your own genes, the immune system of your offspring is particularly diverse, and can fend off a large number of pathogens."

Deceptive mate choice

Strictly speaking, this explanation only applies in every second case, however. Every human and most animals have two – often different – varieties of every individual gene. An egg or sperm cell only receives one of the two gene variants in each case. Some of the cells therefore have immune gene variants that match each other better than others. During fertilisation, an egg cell can therefore in fact merge with a sperm that has been given an MHC variant that does not match so well – despite prior partner selection and what appeared to be the matching immune genes.

The egg – not the woman – must therefore select its own partner, namely the sperm with the complementary MHC variant. According to the researcher team in Plön, this is precisely what the egg cells of sticklebacks do. The scientists presented egg cells with sperm with different MHC variants and observed which of the male gametes was successful. "Our experiments show that the sperm with the highest chance of fertilisation is the sperm whose MHC may differ from that of the egg, but which still shows certain similarities," explains Tobias Lenz, who heads the Evolutionary Immunogenomics research group at the Max Planck Institute in Plön.

The results therefore correlate with earlier studies, which showed that the optimal state for immune defence is provided when two gametes with medium-level differences merge in the MHC. Too large differences are clearly counter-productive, however: "Sperm with only slightly differing MHC variants is more likely to be accepted by the egg cell than sperm with entirely different immune genes," Lenz explains.

Selection after mating

Researchers do not yet know how the egg selects the sperm. "Our experiments show that the selection process continues even after the sex

act. Since it is impossible to tell on the basis of scent which immune gene variants will finally be successful, the selection by the egg cells is an extremely important supplement to partner selection. The offspring are more resistant to pathogens as a result, and therefore have an evolutionary advantage," Milinski explains. Additionally, egg cells can in this way avoid fertilisation by the sperm of unwanted males.

Among fish, with their external fertilisation, which is difficult to control, such free riders are a particular latent problem. However, since selection of the right immune gene was also a decisive factor in the evolution of humans, it would be possible that among humans, egg cells are also involved in deciding which sperm is permitted to fertilise them.

More information: Tobias L. Lenz et al. Cryptic haplotype-specific gamete selection yields offspring with optimal MHC immune genes, *Evolution* (2018). DOI: 10.1111/evo.13591

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