

characterized in yeast might facilitate the capture by or consolidation of protein aggregates into quality control compartments. In conclusion, recent data in yeast are converging on the notion that confinement as opposed to active transport is the primary mechanism to restrict damaged proteins to the altruistic mother, providing a means of quality control for maintaining the vitality of the population.

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Immune Priming: Mothering Males Modulate Immunity

The transfer of immunity from mother to offspring is widespread in animals. The father's contribution to this is usually negligible. However, in a sex-role reversed pipefish where fathers do the mothering, fathers make an important immune priming contribution, too.

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Non-genetic transfer of immunity from mother to offspring is a well-recognized phenomenon known as transgenerational immune priming. Mammals, for instance, exchange immunological information on abundance and composition of pathogens to offspring via the placenta and antibody-rich mother's milk [1], while in fish and insects, mothers are known to make immunological contributions through their eggs [2,3]. Transgenerational defense transfer even occurs in plants [4]. What evolutionary selection pressure is at play here? The paradigm is that offspring who are destined to be raised in a similar disease environment to their mothers will benefit from a maternal enhancement of offspring immunity that reflects the current environmental challenges. The context is a co-evolutionary 'arms-race' between microorganisms and their hosts. As microorganisms evolve stronger virulence, this simultaneously exerts strong evolutionary pressure on hosts to increase their resistance phenotype and genotype [5].

Since it is the female that typically invests time and physical resources in gestating and rearing the young, the investment of transgenerational immunity is both determined and constrained by the maternal immune response. Traditionally, the paternal contribution to immune priming was thought to be negligible. This is because male gametes are considered too small to carry a cargo of immune-modulating proteins such as antibodies [6] and males cannot be guaranteed to share the host-pathogen environment of the offspring.

But what if males were to invest more in nurturing offspring? Would a substantially increased male contribution of physiological resources towards his offspring be accompanied by an augmented male contribution to offspring immune priming? To address these questions experimentally, a model that dissociates the almost invariable link between female gender and high reproductive investment is required.

In contrast to most vertebrate groups where male parental care is rare [7], in fish species that actually look after their offspring, care by males is more often the rule rather than the exception. Selection pressures driving this behaviour may be the greater certainty

of paternity it affords, and the ability of males to care for multiple broods simultaneously without impinging on additional mating opportunities [8]. Of those species with exclusively male parental care, few can match the extreme specialization for looking after offspring seen in the Syngnathids — the group comprising the seadragons, pipefishes and iconic seahorses. In syngnathid fishes, females transfer their yolk-rich eggs to the male during mating, who then take exclusive care of the offspring by osmoregulating and nourishing the developing embryos in remarkably specialized structures located on the male's abdomen or tail [9,10]. The diversity of brooding structures varies among syngnathids, from simple gluing of the eggs to the male's belly through to the sophisticated brood pouches seen in seahorses and some pipefish species [9,10]. Typical of the extreme specialization for parental care seen in this group, the male broad-nosed pipefish *Syngnathus typhle* (Figure 1A) has a placenta-like structure within its brood pouch (Figure 1B) [11,12]. This led Roth *et al.* [13], as reported in a recent issue of *The American Naturalist*, to hypothesize that male pregnancy in *S. typhle* may provide a mechanism for males to selectively contribute to offspring immunity in a manner reflecting the paternal immune experience, and furthermore, that this would be at the expense of maternal contribution to immune priming.

To simulate a pathogenic environment, parental pipefish were exposed to a mix of several phylotypes of heat-killed *Vibrio* bacteria. Immune

response ‘strength’ in the offspring was analyzed by simple enumeration of immune cell populations and by examining mRNA expression levels of selected immune response genes, following their exposure to the same *Vibrio* phylotypes (Figure 1C). Though these parameters are a simplistic assessment of immune strength, within the experimental design they are undoubtedly a reflection of immunological activity and immune system influence. These immunity parameters were compared in offspring from matings where father, mother or both had prior exposure to *Vibrio*. Three patterns of parental contribution to immune priming in offspring were recognized: those contributions that were primed but did not differ whether father, mother or both had been immunochallenged; those that were influenced only when both parents were immunochallenged; or those influenced only by paternal exposure. Hence, in this sex-role reversed scenario, simple dominance of the more nurturing male gender in immune priming is not the whole story.

Roth *et al.* [13] had initially hypothesized that selection for male transfer of immunity to offspring would be more important than selection for female transfer of immunity. This would have been in keeping with their observation from an earlier study on the same species of sex-role reversed pipefish showing that males have a more efficient immune system than females [14], and that offspring born into the environment of the father are more likely to be exposed to the same parasite genotypes. However, although paternal exposure alone affected expression of a few select genes, overall the results point to a far more complex interplay of biparental influences in immune priming.

From a survival perspective, the first scenario, where exposure of either or both parents results in transfer of immunity to offspring, ensures that information on the prevailing microbiological challenges is communicated to offspring with double the likelihood. Roth *et al.* [13] suggest that the second scenario, in which exposure of both parents is required in order to elicit upregulation of immune genes in offspring, reflects a dose-dependence of offspring

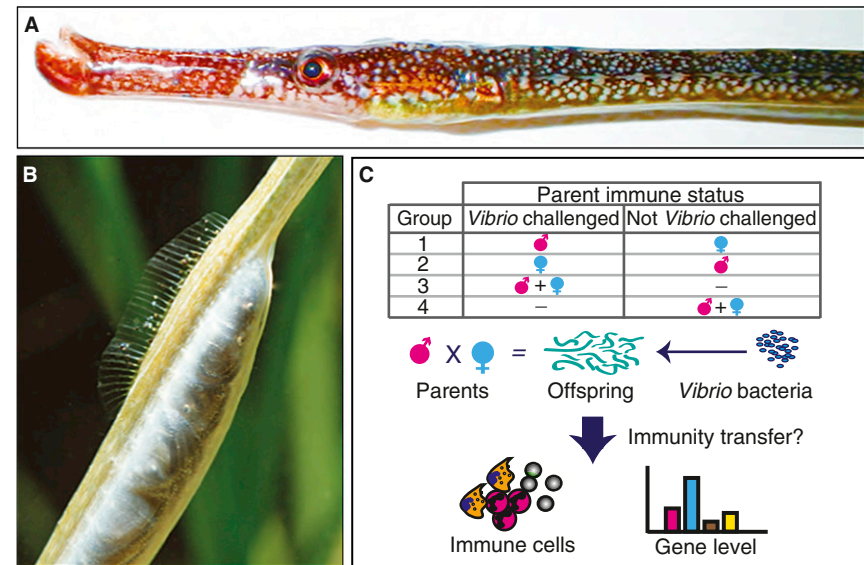


Figure 1. Immune priming in pipefish.

(A) A male broad-nosed pipefish, *Syngnathus typhle*. Photo courtesy of Gry Sagebakken. (B) A gravid *S. typhle* male brood pouch at late gestation. Photo courtesy of Anders Berglund. (C) The methodological approach of Roth *et al.* [12]. Briefly, to determine relative parental contributions to immune priming, males and females with experimentally preconditioned immune status to selected *Vibrio* phylotypes were mated (Table). In the offspring, the immune response following exposure to these same *Vibrio* phylotypes was evaluated.

immunity with a threshold for phenotypic change in offspring that exceeds the dose able to be provided by a single parent. Interestingly, none of the immune parameters tested were affected in offspring by maternal exposure alone, although growth of offspring was significantly increased following maternal immunochallenge. Roth *et al.* [13] argue that this is in keeping with the notion that immune challenged individuals (who will experience a shorter life expectancy due to the costs of investing into enhanced immune defense) ought to invest more heavily into current reproduction as a ‘terminal effort’ [15]. Such an argument would certainly be consistent with a previous study showing that the female pipefish can influence the quality of her offspring by adjusting her investment in egg quality [16].

Traditionally, male ‘pregnancy’ in syngnathid fish is believed to have evolved to increase male reproductive success by nourishing the brood and protecting the developing embryo from potential predators [10]. Given that females must lay their unfertilized eggs directly into the male’s brood pouch, rather than having them fertilized in the

surrounding water, male pregnancy also ensures that a male has complete confidence in the paternity of his offspring [17]. This new study shows that the paternal-offspring relationship of male pregnancy extends beyond the obvious and immediate nurturing roles such as nutrition and osmoregulation. Specifically, the immune priming that male pipefish contribute to offspring provides an additional advantage for the evolution of male pregnancy in this group of fishes.

Since transfer of immunity from fathers to offspring has never been observed in conventional sex-role vertebrate models, syngnathids, which provide variation in both the degree of sex-role reversal [18] and the extent of male pregnancy specialization [9,10], will likely offer insight into whether paternal immune priming was a driver or a consequence of male pregnancy. A more thorough profiling of cytokines, immune cell signalling pathways and functional immunological assays is required to further dissect differences in selection pressure between innate versus adaptive immune responses and the parental dependence of each. Nonetheless, it is clear that extreme specialization for male parental care in

syngnathids provides an important model in which to evaluate features of transgenerational immune priming that are common to all viviparous organisms as well as to study the mechanistic basis of paternal immune priming.

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