to understand disease-associated genes and proteins in their proper context. Although the authors' findings demonstrate the short-term and long-term effects of smoking on cytokine responses in healthy individuals, replication of the study in a clinical setting and with more genetically diverse populations would further aid understanding and modelling of these effects.

This work also highlights the importance of considering other environmental factors that can have both short-term and long-term effects on the immune system. Although some aspects of our immune responses are influenced by inherent factors that cannot be changed — such as age and genetics — other variables, such as smoking, BMI and viral infections, also have a key role in shaping human immune responses.

Taking a step back to consider the bigger picture, epidemiological studies have shown that environmental factors such as smoking and pollution are contributing to a global increase in the prevalence of cancer and cardiovascular and respiratory diseases[4]. However, there is still a lack of detailed understanding about the specific underlying cellular and molecular processes that are influenced by these environmental factors.

Saint-André and colleagues have shown that environmental exposures can affect immune responses associated with cancer through various mechanisms. These mechanisms include 'upstream' changes, such as DNA methylation, and 'downstream' effects on protein abundance. Epigenetic modifications and protein levels, such as those of CEACAM6, are therefore crucial for understanding how environmental exposures result in measurable immune responses. It will be essential to determine how environmental stressors affect epigenetic modifications, gene activity and protein function to better identify and mitigate the effects of environmental exposures on the immune system, and to understand the development of environmentally driven diseases.

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Animal behaviour

How population size shapes fish evolution

Bernt-Erik Sæther

A long-term fish experiment reveals how a mechanism called density dependence, in which the population growth rate slows as the number of individuals rises, affects population dynamics on time scales relevant for ecology and evolution.

As populations grow, a decrease in their growth rate, occurring as a phenomenon referred to as density dependence, affects the dynamics of most species[1]. Writing in *The American Naturalist*, Travis *et al*.[2] provide evidence from guppy fish (*Poecilia reticulata*) on the island of Trinidad that sheds light on the wide-ranging consequences of this type of scenario. The authors demonstrate that variation in population fluctuations can lead to the evolution of large differences in life-history strategies in different populations affecting the pattern of survival of juveniles or adults, the timing of sexual maturity and the numbers of offspring produced.

This research delivers a key finding because most populations in the natural world are affected by this general feedback mechanism — the changes in population size from one point in time to the next depend on the number of individuals present in the population[3]. For nearly 100 years[4] it has been known from theoretical analyses that this type of internal feedback loop should have strong effects on the expected patterns of fluctuations in population size[5]. Density dependence is also known to result in natural selection of certain traits, (for example, the number of eggs produced per season by birds such as the great tit *Parus major*)[6], resulting in evolutionary consequences[7].

Yet, despite its general importance, experimental evidence from natural populations on how density dependence affects dynamic processes, on both ecological and evolutionary time scales, remains rare. Travis and colleagues' study of Trinidadian guppies fills a large gap in this lack of knowledge by experimentally demonstrating how patterns in the fluctuations in population size affect evolution through density-dependent selection, which affects variation in crucial characteristics of the life history of these fish.

The critical age-class[7] is a key concept in studies of evolution in density-regulated populations[8]. This a function that describes the age of individuals in a population at which the strongest regulation of population density occurs. A general prediction from theoretical analyses is that in density-regulated populations, evolution tends to maximize the expected value of the function that determines how the change in the number of individuals is affected by population size[7,8]. For example, the key variable affecting the density-dependent regulation of the size of a population might be either the total number or the total biomass of the individuals present[9].

Testing such effects of density dependence on life evolution in density-regulated populations requires that two conditions are fulfilled[8]. First, the stage of the life cycle that is most strongly affected by fluctuations in population size must be identified. Second, differences in 'fitness' of individuals in terms of the production of offspring (also described as recruits) by individuals must be closely associated with characteristics (phenotypes) that are present at this key stage of the life cycle. An exceptional feature of studying guppies is that they provide a unique opportunity to examine the validity of these key assumptions experimentally.

On Trinidad, guppies (Fig. 1) live in streams where they experience either high or low levels of predation from other species of fish. The composition of these predator communities was previously thought to be the primary selection pressure generating genetic differences underlying the life-history strategies of guppies, which relate to variation in the timing of sexual maturity corresponding to the age and size of the fish[10].

Nearly 15 years ago, the authors moved individual guppies from a high-predation location to generate four new experimental populations subject to two levels (high or low) of resource availability. Because the new populations were initially established using only a few individuals, monthly censuses provided precise estimates of the strength of density dependence. These included how the change in the number of individuals related to the population size; how fluctuations in

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Figure 1 | Trinidadian guppy fish (*Poecilia reticulata*).

the total biomass of the population (measured by weighing the fish) affected seasonal variation in the probability of an individual's survival from one month to the next; and the number of individuals produced per female (the recruitment rate).

This experimental set-up produced a remarkably clear set of results. First, in all four populations, a model for the data that included density dependence fitted the data better than models that did not ('random walk' models). This provides evidence that the regulation of the population growth rate was influenced by the total biomass of fish in each population in three of the four populations. However, the authors did not find a 'steady state' consistent with regulation in the fourth population. Such long-term experimental studies of population dynamics are rare in ecology[11].

Second, the density dependence acting on the change in population size occurred through a consistent decline in recruitment rates associated with a rise in the total biomass. By contrast, adult survival was unaffected by an increase in biomass.

Thus, these data indicate that juveniles are the critical age-class[7,8] for regulating the size of these populations, because juvenile survival influences the individual fitness of adults in terms of the number of new recruits produced. Consequently, increased biomass decreased the high reproductive rate of adults and the juvenile survival rates, whereas adult survival rates were independent of biomass. This indicates strong density-dependent selection for delayed sexual maturation when population biomass is high[7,8]. Surprisingly, the presence of a competing species, the killifish (*Rivulus hartii*) had only minor effects on survival and recruitment rates for guppies, indicating that the major selection pressure for delayed sexual maturation was related to a reduction in food availability when fish biomass was high.

The authors' experiments have generated many questions, one of which is how the adults' ability to produce new recruits at different resource levels is related to their own phenotypes or the phenotypic characteristics of the juveniles. Analyses of how the average fitness of individuals depends on traits such as body mass might provide evidence for a phenotype that maximizes the average fitness in the population[12]. However, the characteristics of an optimal phenotype might differ between populations: the authors found inter-population variation for the strength of density dependence, the degree of environmental fluctuations and resource availability. Another central question is whether density-dependent selection that influences the age of maturity[10] will cause correlated changes to traits at later life stages, which affect the degree of reproductive success or survival at older ages.

A clear message arising from this study is that understanding the capacity for natural populations to adaptively evolve in response to new environments must include density-dependent selection to provide realistic conclusions. This study also provides evidence for the suggestion[13] that density-dependent processes can be a key selective agent in determining differences in life-history strategies that arise within a species or between different species.

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