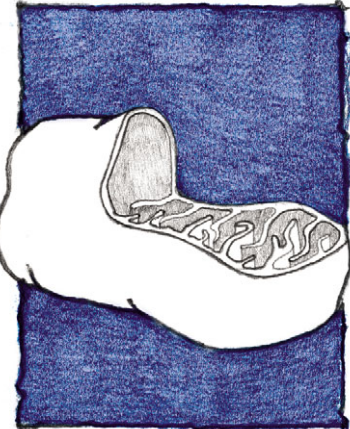


MITOCHONDRIAL DNA



**GENES FOR THE LONG RUN**

Can the same genes both improve your aptitude for endurance exercise and lower your life expectancy? A recent study of mitochondrial DNA (mtDNA) in track athletes suggests that the answer may be 'yes'.

The mitochondrial genome is a small (17-kb), circular chromosome that encodes 13 components of the electron transport chain, which generate the proton gradient necessary for aerobic ATP production. Mitochondrial DNA might therefore be expected to influence an individual's ability to sustain long periods of exercise. To determine whether the mitochondrial genes of track athletes differ systematically from those of the population at large, Niemi and Majamaa analyzed the mtDNA sequences of 141 elite Finnish long-distance runners and sprinters as well as 1060 Finnish control subjects. They found that certain groups of mtDNA sequences (called haplogroups, since there is only one copy of the chromosome per mitochondrion) occurred less frequently in the distance runners than in the sprinters and control subjects. In particular, no distance runner belonged to haplogroup K or subhaplogroup J2, whose combined frequency is at least 4.5% among control subjects and is even higher among sprinters.

Since distance runners are heavily dependent on aerobic ATP production by their mitochondria, it isn't surprising that their mtDNA differs from that of people with different exercise habits. For example, genes for protein isoforms that mildly impair ATP synthesis should presumably be rare among endurance athletes. What's interesting, however, is that the haplogroups underrepresented among the distance runners are overrepresented among very old people. Previous work by

the Niemi/Majamaa group and others has shown that members of haplogroup K and subhaplogroup J2 tend to live longer than people of other haplogroups.

Is it plausible that the mitochondrial genes of haplogroup K and subhaplogroup J2 limit endurance performance but improve life expectancy? Niemi and Majamaa offer an intriguing hypothesis to explain this potential paradox: perhaps J2 and K are 'uncoupling genomes' that increase proton leak across the mitochondrial membrane. An elevated proton leak could certainly limit aerobic ATP production, and thus endurance performance. But it could also prevent the mitochondrial membrane potential from rising into the range (>140 mV) where production of reactive oxygen species (ROS) becomes high. ROS have been implicated in ageing, so limiting ROS production could contribute to a longer life. Although the link between ROS and ageing is still under investigation, several mouse studies have suggested that relatively 'leaky' mitochondria could promote longevity by minimizing the generation of ROS. Thus, if members of J2 and K haplotypes limit their ROS production, this could explain why they live longer than other people.

If the rareness of J2 and K among endurance athletes is confirmed by additional work, the 'uncoupling genome' hypothesis should be tested with biochemical measurements of mitochondria isolated from representatives of different haplogroups. If the hypothesis is correct, mitochondria of haplogroup K and subhaplogroup J2 should have lower membrane potentials, lower ROS production rates and lower ATP production rates (relative to O<sub>2</sub> consumption rates) than other mitochondria. Such studies would represent the completion of another lap in our race to understand the genetic basis of differences in athletic performance.

10.1242/jeb.01802

Niemi, A. K. and Majamaa, K. (2005). Mitochondrial DNA and ACTN3 genotypes in Finnish elite endurance and sprint athletes. *Eur. J. Hum. Gen.* **13**, 965-969.

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CASTE SYSTEM



**A CINDERELLA STORY**

In human societies, not everyone is born equal. The phrase 'born with a silver spoon in the mouth' refers to the fact that, at birth, some people find themselves in positions of privilege and wealth whereas others do not. Similar inequalities exist within animal societies and, in the case of some insects such as ants and bees, are taken to great extremes. Ants and bees have evolved eusociality – several generations live together in colonies, only one or a few individuals (queens) have offspring, and non-reproductive colony members, the workers, care for these offspring. Becoming a queen is not something that workers can aspire to. Although some sneaky workers do try to have offspring themselves, individuals born as workers cannot become queens. Nutrition is an important determinant of social class in many eusocial insect species. In some species, larvae destined to become queens are fed a particular substance (royal jelly in honey bees), whereas in other species queen larvae get more food than worker larvae. This latter system is found in the stingless bee *Schwarziana quadripunctata*. Now, an international team of researchers from Belgium, Britain and Brazil led by Tom Wenseleers has discovered that some stingless bees manage to beat the system and change their fate.

The team investigated previous reports that dwarf queens occur in stingless bee colonies in addition to the normal, large queens. Wenseleers and his co-workers weighed the dwarf queens and showed that they are indistinguishable in weight from regular worker bees. In addition, dwarf queen larvae are raised in cells that are identical to the cells in which worker larvae are raised, which are smaller than the large specialized cells in which the queen larvae develop. Dwarf queens aren't a rare occurrence; when the team assessed the social class of 11 574 individual

stingless bees from 19 colonies, they found six times more dwarf queens than normal queens. The team used a series of morphological measurements to identify adult dwarf queens and distinguish them from normal queens. They showed that the dwarf queens headed 12 out of a further 54 colonies, suggesting that the dwarf queens are able to reproduce. Although this may seem like a large proportion of colonies, it actually suggests that dwarf queens aren't as successful as normal queens – 86% of queens reared were dwarf queens, but they only headed 22% of the colonies that the team studied. Wenseleers and his co-workers suggest that this discrepancy may be due to workers actively discriminating against the dwarf queens.

Many questions remain about this intriguing system in which individuals seem able to choose whether to become queens. In particular, it would be interesting to know exactly which mechanisms determine the fate of stingless bee larvae. What role does nutrition play in determining their fate? If nutrition determines whether an individual becomes a queen or a worker, then some larvae destined to become workers are apparently overcoming nutritional limits and becoming queens despite their limited food supply. What physiological mechanisms control nutritional responses in this system? Recent advances in *Drosophila* have given us some places to start looking for answers, such as insulin receptor pathways. Perhaps these or other, as yet unknown, pathways play a role in the production of dwarf queens in stingless bee colonies. Whatever the case, this system has the potential to keep ecologists and physiologists busy for many years to come.

10.1242/jeb.01804

Wenseleers, T., Ratnieks, F. L. W., Ribeiro, M. de F., Alves, D. de A. and Imperatriz-Fonseca, V.-L. (2005). Working-class royalty: bees beat the caste system. *Biol. Lett.* **1**, 125-128.

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## PYTHON'S HEARTY MEAL

Carnivorous reptiles exhibit a massive increase in oxygen demand following a meal to meet the increased metabolic demands associated with digestion. Inherently, this increase in oxygen demand places an extra demand on the cardiovascular system; the heart needs to work harder to transport more oxygen to the metabolically active digestive organs. Pythons appear to deal with this increased cardiac demand by substantially increasing the mass of their heart (cardiac hypertrophy) within two days of feeding. But just how do these snakes manage to pump up their heart's mass?

Andersen and colleagues at the University of California, Irvine, were interested in determining the cause of the cardiac hypertrophy following feeding in the python (*Python molurus*). They wanted to know if the increase in heart mass was due to increased protein synthesis (i.e. formation of new heart muscle) or a water shift between extracellular and intracellular compartments, leading to increased fluid content of the heart tissues. In order to investigate this, Andersen and colleagues obtained ventricles from three groups of pythons: (1) fasting (these snakes had been fasted for 28 days); (2) digesting (these animals had digested a large meal 2 days earlier); and (3) post-digestive (these pythons had digested a large meal 28 days earlier). For each of these groups, the team measured ventricular dry/wet mass ratio, the ventricle's total protein, RNA and myofibrillar protein concentrations on a mass-specific basis, and the expression of messenger RNA for heavy-chain cardiac myosin, a contractile element of the heart.

As they expected, the team observed a 40% increase in pythons' ventricular mass during digestion. They identified several clues that this hypertrophy was due to *de novo* protein synthesis and not increased

fluid content of the heart. Primarily, the team found that the expression of messenger RNA for heavy-chain cardiac myosin increased significantly 2 days after feeding, indicating that digesting snakes synthesise myosin. Further, they discovered that the hearts' mass-specific total protein, RNA and myofibrillar protein concentrations did not change during digestion. In other words, as the pythons' hearts increased in mass after feeding, the ratio of protein to heart mass remained the same, indicating that new protein was being formed as the hearts expanded. This finding also ruled out increased water content as an explanation for the cardiac hypertrophy; if the increased heart mass was due to an increase in fluid content, these mass-specific protein concentrations would have decreased. Finally, they found that ventricular dry/wet mass ratio did not differ between fasted and fed snakes, providing further evidence that the larger hearts were not due to increased water content. The team concluded that the cardiac hypertrophy observed in digesting pythons is due to the synthesis of new contractile protein.

Additionally, the team showed that the increase in heart mass during digestion was a fully reversible process. The mass of post-digestive snakes' hearts was similar to the mass of fasted snakes' hearts. Thus, following a meal, a python can rapidly increase its heart size by 40% and then decrease it again within 28 days. In comparison with mammalian species, in which comparable increments in ventricular size take weeks to develop, this cardiac remodelling occurs very rapidly. As such, Andersen and colleagues stress that this natural, rapidly occurring and fully reversible cardiac hypertrophy could provide a useful model for investigating the mechanisms that lead to cardiac remodelling and growth in other animals.

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Andersen, J. B., Rourke, B. C., Caiozzo, V. J., Bennet, A. E. and Hicks, J. W. (2005). Postprandial cardiac hypertrophy in pythons. *Nature* **434**, 37-38.

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