Genetic control of the seasonal reproductive cycle in micromammals

By

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SUMMARY
(Genetic control of the seasonal reproductive cycle in micromammals)

Seasonal breeding is the process by which species of the temperate zones of the Earth concentrate the reproductive effort in those seasons in which environmental conditions are more favorable. In seasonal breeding mammals, both female and male gonads undergo substantial changes during the transition periods between the breeding and the non-breeding periods, but these processes have been studied in very few species to date, so that the mechanisms of gonad inactivation are not well understood yet. Moreover, most studies are incomplete as only one particular aspect of the entire process was focused in many cases (apoptosis, hormonal variations, ultrastructure, morphological changes, and dynamics of cell adhesion molecules). Comprehensive studies including all these features have been performed only in the Iberian mole and the long hairy armadillo. Hence, additional seasonal breeding mammalian species must be investigated in order to elucidate if there is a conserved mechanism of testis regression in mammals or there are several alternative mechanisms that can operate in different species or circumstances. Micro-mammals are ideal species for this kind of studies as multiple captures of wild animals have to be done in order to get statistical significance in the comparisons between different seasons required for many reproductive parameters.

In the present work we investigated for two years four mammalian species, the greater white-toothed shrew, *Crocidura russula*, the Algerian mouse, *Mus spretus*, the wood mouse, *Apodemus sylvaticus* and the Mediterranean pine vole *Microtus duodecimcostatus*, in order to study 1) whether these species experience seasonal breeding, 2) the functional status of the main cell types (Sertoli, Leydig, peritubular myoid and germ cells), structures (seminiferous tubules, lamina propria), and biological processes (spermatogenesis) throughout the seasonal reproductive cycle, 3) the spatio-temporal pattern of expression of several genes involved in testis function, 4) the androgenic function of the testes, 5) the role of both apoptosis and cell proliferation in the process of testis regression, 6) the role of cell junctions in the seasonal dynamics of the germ cells, and 7) the possible existence of associations between altered gene expression patterns and seasonal testis regression in these species, in order to establish possible roles for these genes in the control of seasonal breeding.

We found that differences between species, reflect some species-specific differences in gene regulation. Summer testis regression was detected

in *A. sylvaticus* and *M. duodecimcostatus*, which showed very different levels of apoptosis in the inactive testis, being very high in the former and very low in the latter species. Our results in *A. sylvaticus* and those reported previously for *T. occidentalis* suggest that the role of apoptosis in the inactive testes is to eliminate the germ cells that continue entering meiosis during the non-breeding period. However, the case of *M. duodecimcostatus* is exceptional because in this species the frequency of apoptotic cells decreases during testis regression. Nevertheless, data from this species also support the hypothesis as the number of germ cells entering meiosis in their inactive testis is also very low if compared with that of *A. sylvaticus* we found that several features of the regressed testes in seasonal breeding males are quite well conserved from an evolutionary point of view.

Our results evidence that in the studied populations seasonal breeding is not a species-specific feature. Rather, it depends on the life conditions that every particular individual is facing at each moment. Hence, it appears that these animals show a clear tendency to reproduce continuously at all seasons, but the environmental cues concomitant with a particular climatic season at a given latitude force them to stop breeding. Two extreme situations can be recognized in mammals regarding the control of circannual reproduction timing: 1) species in which the hypothalamus-pituitary-gonad axis is tightly regulated by the photoperiod and exhibit constant and rigid seasonal breeding patterns; 2) species with opportunistic seasonal breeding, in which photoperiod has little or no influence in their reproduction timing, which mainly depends on micro-environmental cues like water and food availability, temperature, rainfall, etc. European moles, lemmings, hamsters, deers, brown bears, and many other species living in central and northern Europe and similar latitudes in North America and Asia, probably belong to the first group. The greater white-toothed shrew and the Mediterranean pine vole and probably many other species whose area of distribution extends toward lower latitude regions, belong to the second group.

All four species analyzed in the present study showed at least one peculiarity in their reproductive biology that makes them different from each other. These multiple species-specific models of circannual testis variation in seasonal breeding species suggest 1) that the mechanisms controlling seasonal reproduction are in fact very plastic and much less rigid than initially considered, and 2) that they appear to be fast evolving. Hence, mammalian populations probably have available multiple ways to get adapted to the unstable environmental conditions that the climate change will probably cause in the future.