reduction in proliferative capacity, in the context of a tumor microenvironment where nutrient levels vary spatially, migration might still lead to an overall increase in the number of progeny a cell leaves behind relative to a completely undifferentiated competitor since it can now escape hostile microenvironments [6]. One of the hallmarks of malignancy is the ability to migrate, locally invade and distantly metastasize. If the CSC hypothesis is true and Bruggeman et al.'s findings in glioblastoma hold up in other solid tumors, the interruption of cell differentiation might, quite counter-intuitively, lead to more benign tumor behavior.

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Vomiting is not an adaption for glaucoma (and Darwinian medicine is difficult)

A recent paper in *Medical Hypotheses* [1] suggests that vomiting in acute angle closure glaucoma (AACG) ''should not be seen as a symptom of disease but rather as a complex adaptation which has evolved in response to the anatomical predispositions to AACG in the camera type eye''.

Evolutionary hypotheses are welcome, but they should be published only if they are consistent with existing evidence and theory. This one is not. First, vomiting would not change the electrolyte balance enough or fast enough to reduce intra-ocular pressure. Second, vomiting is by no means universal in AACG. Third, AACG is too rare to shape a specific defense mechanism. Fourth, AACG is most common in elderly patients in their sixth and seventh decades of life, an age at which selection was essentially absent in evolving human populations. Finally, alternative hypotheses are available. For example, pain can cause vomiting. Also, acute glaucoma stimulates the trigeminal cranial nerve which has connections with the descending branch of the longitudinal fasciculus of the tenth nucleus [2].

Evolutionary applications to medicine are growing fast, and new ideas and investigators are welcome. However, without evolutionary biologist collaborators, it can be difficult to distinguish viable from nonviable hypotheses. Publication of hypotheses that are inconsistent with facts and theory can leave the impression that standards of evidence in Darwinian medicine are different from those in the rest of medicine. They are not. Special difficulties apply, but these led to specific suggestions about how to go about testing evolutionary hypotheses in medicine [3].

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Mad Neanderthal disease? Some comments on ''A potential role for Transmissible Spongiform Encephalopathies in Neanderthal extinction''

Underdown [1] proposes that Transmissible Spongiform Encephalopathies (TSEs) played an important role in Neanderthal extinction. While original, this idea is unsupported by a critical review of the relevant data. First, referring to the Fore in this context is problematic: they are horticulturalists, a poor analog for mobile hunter-gatherers; the *kuru* epidemic unfolded over only decades, whereas Underdown postulates that TSEs would have plagued Neanderthals for millennia; and Fore population densities are several orders of magnitude greater than those of Neanderthals [2], with concomitant epidemiological implications.

Second, the 'kuru Model' is based on *only one case*, and not all cannibalism needs result in the development and rapid transmission of TSEs among its practitioners. Is it realistic to extrapolate from one documented instance (among modern humans) to the entirety of Neanderthals? It is not warranted to consider Neanderthals as a homogeneous whole when it is unarguable that they displayed a great deal of behavioral flexibility throughout their range.

Third, the best-known cases of Neanderthal cannibalism (Krapina and Moula-Guercy) date to 100—80 kya, and there is little evidence of it after that. While anthropic modifications of Neanderthal remains are reported from El Sidrón [3], they may not reflect cannibalism since comparative studies on the treatment of associated animal remains are unavailable. Thus, there is little evidence that Neanderthal cannibalism was a widespread practice for the 50 ky leading up to their disappearance, a period during which Mousterian sites appear to have increased in density as opposed to the steady decrease implied by Underdown [4].

Lastly, there is clear evidence of perimortem processing of *Homo sapiens* remains with stone tools: human teeth from four Aurignacian deposits were forcefully removed from their gums and transformed into ornaments [5], and human skulls from at least three Middle Stone Age sites bear traces of defleshing [6—8]. Since Underdown states that TSEs might have been transmitted ''through cuts caused by stone tools used by infected and non-infected individuals'', should we not assume that TSEs must have been a concern for modern humans as well?

In sum, while TSEs may have affected some groups of Neanderthals *and of modern humans*, short of having identified them genetically, there is no reason to suggest that they were an especially important factor in the disappearance of Neanderthals.

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