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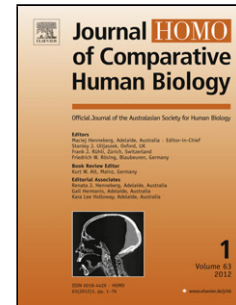
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What to expect from an evolutionary hypothesis for a human disease: the case of type 2 diabetes

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Abstract

Evolutionary medicine has a promise to bring in a conceptual revolution in medicine. However, as yet the field does not have the same theoretical rigor as that of many other fields in evolutionary studies. We discuss here with reference to type 2 *diabetes mellitus* (T2DM) what role an evolutionary hypothesis should play in the development of thinking in medicine. Starting with the thrifty gene hypothesis, evolutionary thinking in T2DM has undergone several transitions, modifications and refinements of the thrift family of hypotheses. In addition alternative hypotheses independent of thrift are also suggested. However, most hypotheses look at partial pictures; make selective use of supportive data ignoring inconvenient truths. Most hypotheses look at a superficial picture and avoid getting into the intricacies of underlying molecular, neuronal and physiological processes. Very few hypotheses have suggested clinical implications and none of them have been tested with randomized clinical trials. In the meanwhile the concepts in the pathophysiology of T2DM are undergoing radical changes and evolutionary hypotheses need to take them into account. We suggest an approach and a set of criteria to evaluate the relative merits of the alternative hypotheses. A number of hypotheses are likely to fail when critically evaluated against these criteria. It is possible that more than one selective process are at work in the evolution of propensity to T2DM, but the intercompatibility of the alternative selective forces and their relative contribution needs to be examined. The approach we describe could potentially lead

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