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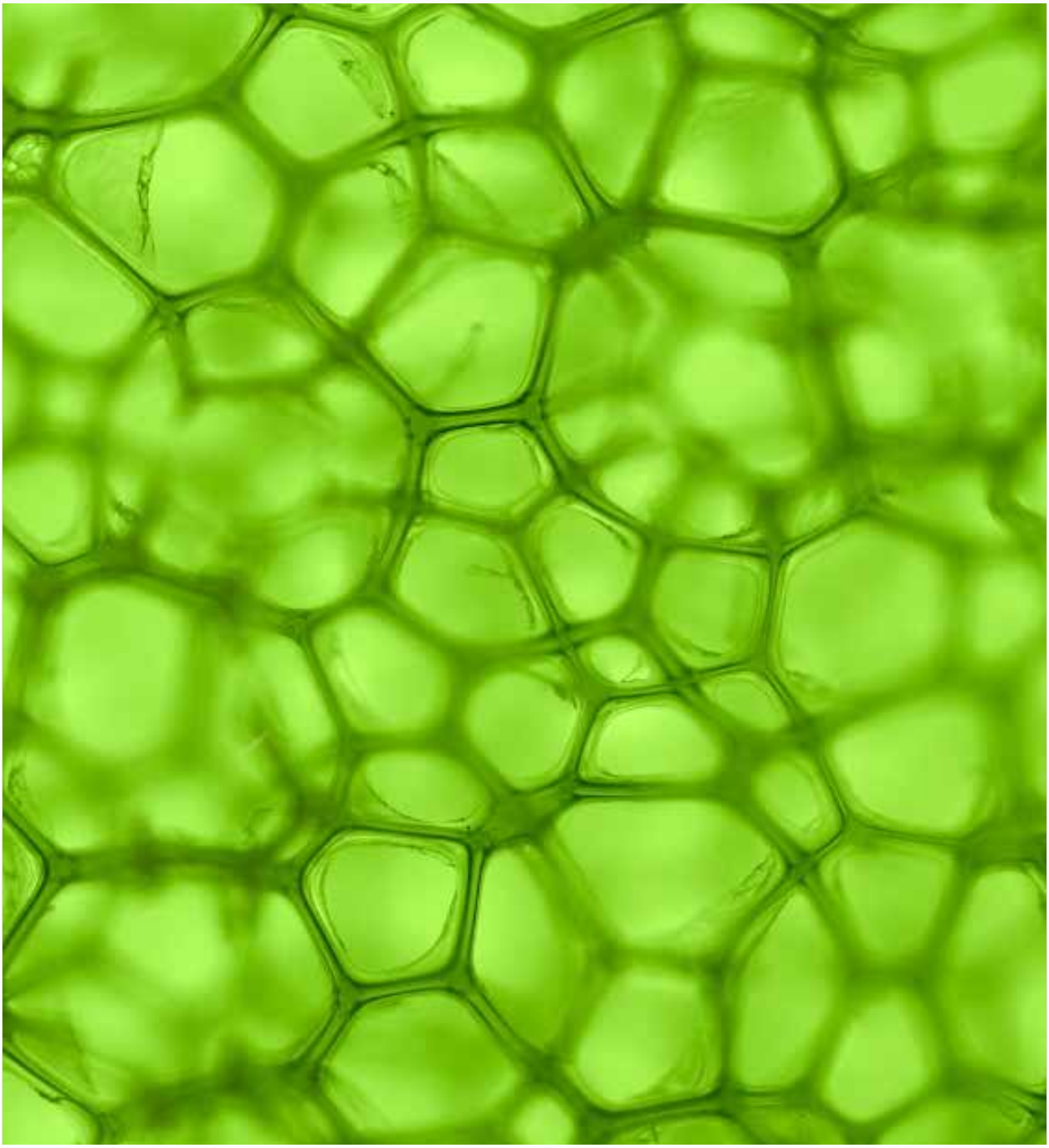

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# Brief History of Biologic Innovation

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Early organisms were biologically immortal—meaning that they could persist indefinitely through homeostasis. Necrotic death was something that happened when an organism became overwhelmed by stress. Innovation largely occurred through the selection and reproduction of genes.

One of the most powerful innovations to occur during primordial evolution was programmed cell death (PCD), a cooperative function that promotes fitness in certain contexts.[1] [2] Heritable PCD is associated with the emergence of social species and multi-cellular organisms through multi-level selection.

Predation is another early biologic innovation that served as a powerful driver of evolution. From a multi-level selection perspective, predation was a strong force in terminating less fit traits.[3] The rise of predation is associated with explosive speciation during the Cambrian period.

Cognitive innovation enabled the rise of memes as a powerful force in trait acquisition.[4] Memes have many features that are advantageous over genes in the acquisition of behavioral traits that promote fitness. Whereas gene propagation largely occurs vertically down generations, memes propagation is much more versatile. Memes can be acquired bi-directionally up and down generations, horizontally within a generation, and over large distances. Trait selection based on gene requires formation of variations and selection against weak traits through recycling of physical components–a thermodynamically

expensive process. Trait selection based on memes occurs far more efficiently and at negligible biologic cost.

For trait acquisition through memes, death represents a bottleneck. Each generation is forced to transfer memes to the next generation through education before dying off. Whereas dying promotes trait evolution through genes, living promotes trait acquisition through memes. In a way, human aspirations for longer lifespan are in line with the shifting balance of power from genes to memes in the evolution of traits.

In the search for methods of lengthening human lifespan, one consideration looms large: the possibility that programmed death is a feature of multi-cellular organisms, inherited from unicellular predecessors either because of little selection pressure against it or selection pressure for it. At the very least, if programmed organism death has indeed been inherited as some would suggest, it would be maladaptive for meme accumulation.

Indeed, the apparatus for PCD has persisted through the evolution of eukaryotes and multi-cellular organisms to this day.[5] PCD in the pineal gland and hypothalamus appears to engender organism-wide regulatory dysfunctions over time that age the body after puberty and ultimately kill it.[6] Aging-related diseases can be viewed as an epiphenomenon of a process that was inherited, and possibly selected, for during evolutionary history.[7] [8] [9] [10] Can programmed death be reprogrammed and eliminated? Cancerous transformation offers a tantalizing natural example of the possibility that PCD can be eliminated.

In the long view, the narrative of human evolution may one day be seen as the transition species that innovated memes to both end genetic evolution and accelerate meme-based evolution–a path without programmed death or death from biotic stress (predation, infection). Some of those memes—healthcare innovations—are

already extending human lifespan, thereby lengthening the period of meme acquisition per organism and increasing the overlap between human generations.

In summary: (1) programmed cell death was an early innovation in the evolution of traits through genes; (2) memes emerged as an alternative means to promote trait acquisition, a process undermined by death; and (3) healthcare has emerged as a uniquely human innovation to delay and ultimately perhaps even terminate death. Human genetic evolution would then slow and possibly end. The post-Darwinian era has begun.

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# The Grand Bargain

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Pascal's Wager posits that since more can be gained from betting on the existence of God than on atheism, a rational person should live as though God exists even in the absence of evidence. Put another way, the cost of being wrong about the existence of God is much higher if one bets against the existence than if one bets for it. What would be the analogous wager in the debate about the existence of programmed organism death (POD), also known as phenoptosis?

Since the idea was first widely publicized by August Weismann over a hundred years ago, the notion of phenoptosis has inspired vigorous debate, particularly among those who oppose it. The opposition is based both on theoretical grounds as well as the issue of empirical evidence supporting the existence of phenoptosis. On the theoretical side, the argument against phenoptosis centers on whether phenoptosis as a heritable trait can actually promote fitness. On the empirical side, the argument against phenoptosis centers on the lack of consensus acceptance of mechanisms that could execute self-termination across all aging species–something akin to apoptotic pathways in cell suicide. Counterarguments to these objections are addressed elsewhere.

Viewed through the lens of Pascal's Wager, we argue that more can be gained from betting on the existence of phenoptosis than betting against it. The current wisdom, which assumes the latter, is to treat aging and age-related diseases as a set of dysfunctions that emerge through absence of selection against them. The diagnostic and treatment paradigms based on that understanding can be best characterized as inefficient, expensive, and ultimately ineffective, since everyone still

dies in the end despite all attempts and aspirations for staying alive.

If we assume that programmed death is wired into the biology of humans, as well as that of virtually all multi-cellular organisms, that assumption opens up the possibility that the pathways of phenoptosis can be reprogrammed to enable persistent health. While the field of medicine continues to toil away at finding Whack-a-Mole™ solutions to aging-related diseases, looking for and eliminating the death program might be a holy-grail shortcut solution around the entire healthcare field.

The risk of creating a healthcare research field around phenoptosis is high as it could lead to diversion of critical resources. However, we argue that the risk of not creating it is a lot higher. Thus, we put forth Weismann's Wager, a notion that a rational scientific society would endeavor as though phenoptosis existed even in the absence of evidence. Winning Weismann's Wager and conquering programmed death would dramatically reduce the need to contemplate Pascal's Wager.

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