Klotho and Pulmonary Hypertension
Spinning a Yarn or the Thread of Life?

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In the ancient Greek mythology, Klotho was the youngest of the 3 Fates responsible for spinning the thread of human life. Her sister Lachesis was thought to draw the lots and determine how long one lives by measuring the thread of life, and her other sister Atropos chose how someone dies by cutting the thread of life with her shears. Klotho was the youngest, and she had the power to make major decisions in not only choosing who was born but also determining if a mortal should be saved or put to death. The 3 Fates (or the Moirai) were believed to appear 3 nights after a child’s birth to determine the course of its life.

When a new gene, thought to be involved in the suppression of ageing, was discovered in 1997,1 it was named Klotho after the youngest sister of these 3 Fates. In their article, Varshney et al2 report that stem cell delivery of secreted Klotho prevented monocrotaline (MCT)-induced endothelial dysfunction and pulmonary arterial remodeling, perhaps by reducing inflammation, restoring levels of SIRT1 (Sirtuin 1; deacetylates proteins that contribute to cellular regulation) and endothelial nitric oxide synthase. The distribution of the transfected gene in the lung was not clear but would be of interest.

So, does Klotho spin new hope for life after pulmonary arterial hypertension (PAH)? We certainly hope so. It is certainly intriguing as a new potential therapy—but wait—are we not all by now a little wary of the fact that most experimental treatments seem to reverse or prevent pulmonary vascular damage and pulmonary hypertension (PH) in this model? Many agents (over 50) have been reported to prevent or reverse established MCT-induced PH, but only endothelin-1–antagonists,3 PDE5 (phosphodiesterase 5) inhibitors,4,5 and prostacyclin6 or prostacyclin analogues7 have translated into the clinic to date. So what are The Fates for PAH patients? Survival in patients with PAH is still poor, and so, if you believe in Greek mythology, they may be too well acquainted to Atropos and have too much influence from Lachesis. We hope, however, that the younger sister Klotho will indeed spin the thread of life for PAH patients. Time will tell.
References


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