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OBITUARY

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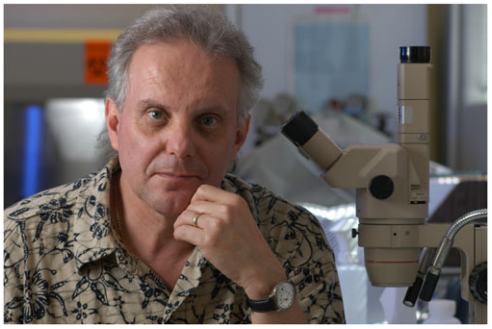
A remembrance of Dr Panagiotis A Tsonis (1953–2016)



Dr Panagiotos Tsonis, lovingly addressed as 'Takis' by his friends, a renowned regeneration researcher, died on 3 September 2016 at the age of 63 as a result of a massive heart attack. Takis was born in Greece to Antonios Tsonis and Isidora Tsonis. He was among the most influential regeneration scientists in the past 30 years. He received his BSc from the Department of Biology, University of Patras, Greece, in 1976. He received his MSc and PhD from the Institute of Molecular Biology, Nagoya University, Japan, in 1983.

Takis was fascinated by Greek mythology, in particular Prometheus, the Greek Titan, whose immortal liver was feasted on day after day by Zeus's eagle, and it regenerated again every time. The myth raised an important question of modern history: did the ancient Greeks know about the liver's amazing capacity for regeneration? Given the strong influence of Greek history and mythology, it is not surprising that Takis embarked on a career in the field of regeneration. He moved to Japan on a research fellowship to work on an exotic, but less known, animal model at that time: the newt or salamander that possesses amazing regenerative abilities. He was the first Greek citizen to receive a PhD degree from a former Japanese Imperial University. The title of his Master's thesis was 'Effects of carcinogens on regenerating and non-regenerating limbs in adult newts,' under the supervision of Professor Goro Eguchi. He continued his work on understanding regeneration for his PhD degree, continuing his studies on the effects of carcinogens on regeneration. His studies unraveled a very interesting observation that this animal has evolved such a perfect, tightly regulated growth regimen during regeneration that even exposure to carcinogens does not result in tumor production, which was an important milestone in the field (Tsonis & Eguchi, 1982, 1983; Tsonis, 1983). It resulted in a new direction in the field of regeneration where researchers started using the newt model to understand how regeneration is regulated at the molecular genetics level, and further how the newt controls the size of the regenerate and defies the problem of tumors or abnormal growth associated with regeneration.

After his PhD, Takis continued his passion for regeneration research at postdoctoral level at La Jolla Cancer Research Centre. Takis then moved to the Department of Medicine at Indiana University to further his research interest in regeneration in newts. He moved to the University of Dayton in 1989 and continued his research career here. Takis was fascinated by the fact that newts/salamander possess a unique capacity to reprogram adult somatic cells to a more embryonic progenitor state during regeneration. Recently, his laboratory has been devoted to understanding the molecular genetic underpinning of lens and limb regeneration using functional genomic approaches in the versatile newt model. He believed that understanding the molecular mechanisms will have a major impact on human health.

Takis published several highly acclaimed books, compilations of lectures and nearly 190 peer-reviewed publications that have been cited more than 4200 times. Among his most notable contributions to the field, Tsonis and his group developed a model for lens regeneration in newts (Tsonis, Madhavan, Tancous, & Del Rio-Tsonis, 2004). It was known that the dorsal pigmented epithelial cells of the iris can dedifferentiate and then differentiate to form a new lens. However, the molecular mechanisms of this process were unknown. Tsonis's group determined that one of the differences in dorsal versus ventral iris cells was due to differences in BMP signaling. Furthermore, they determined differences in gene expression between the dorsal and ventral iris building a genetic basis of dorso-ventral constraint in lens regeneration (Grogg et al., 2005). This paper proved to be a major milestone in the field of regeneration showing induction of lens regeneration from the non-competent ventral iris. Newts have the ability to regenerate their lens during their adult life. Tsonis's group showed that newts can withstand repeated lens regeneration, even at old age, resulting in lenses structurally and transcriptionally similar to young newt lenses that have never experienced regeneration (Eguchi et al., 2011). His group also compared transcriptomes of lenses, irises, and tails from aged newts that had undergone lens regeneration 19 times and demonstrated that, despite aging, the gene expression of regenerated lenses does not exhibit any deviation in the robust transcriptional program compared to young and intact lenses (Eguchi et al., 2011; Sousounis et al., 2015). Recently, he, along with his collaborators, demonstrated that the newt can regenerate its limbs throughout its life by switching cellular mechanism from a stem cell based mechanism during larval stages to a dedifferentiation based mode in the adult (Tanaka et al., 2016). Takis was trying to bridge the information from classical biology to molecular/genetic, high throughput approaches in different models of regeneration (Tsonis, 2007; Sousounis, Baddour, & Tsonis, 2014). Most recently, evolution of the eye and lens caught his interest and he utilized information from his transcriptome analysis to understand the evolution of the pinhole eye and the role of Six-3, a master regulator of eye development (Singh & Tsonis, 2010; Ogura et al., 2013).

Dr. Panagiotis Tsonis, a renowned regeneration scientist. Photo taken in newt regeneration laboratory at University of Dayton.

Takis had a vision for promoting research and was instrumental in developing a Centre for Tissue Research and Engineering at Dayton (TREND) at the University of Dayton, which was subsequently declared by the state of Ohio as one of the Centers for Excellence in Research. The TREND Center supported research collaborations between university faculty and research scientists and engineers in the area of tissue regeneration and bioengineering with the aim of understanding the basic biology of how damaged tissues and organs can regenerate. This center will be one of the landmarks for his legacy in regeneration research at the University of Dayton.

Throughout his career, Takis showed a commitment to training the next generation of scientists by mentoring them in research and teaching them in the classroom. He taught molecular biology to graduate and undergraduate students using his published book on *Anatomy of Gene Regulation* (Tsonis, 2003). He received several awards for his outstanding scholarship. He also served the community by serving on editorial boards of journals in his fields and grant review panels.

Takis embodied the love of family, friends, and passion for science equally, which was further supplemented with his great sense of humor. Takis was a great mentor to students and post docs in his laboratory as well as junior faculty (including me) in the department. As an ardent reader and hands-on person, he always challenged his students through research problems and historical perspective of the topics.

Apart from his accomplishments as a scientist, Takis was a big fan of the Greek soccer team Olympiacos F.C. and was a long-time San Diego Chargers fan. Takis was a world traveler and a connoisseur of arts and poems. He had an extensive collection of excellent literature from all over the world in his study. His first compilation of his poetry will be published soon. Among his friends and family, he will be remembered as a great human being with a kind heart, infinite intelligence, and sense of humor, and also for his gourmet cooking, eclectic musical taste, love for poetry and passion for traveling throughout the world.

Takis is survived by his wife and life-long collaborator Katia Del Rio-Tsonis, his two daughters Isidora Margioras and Sol Tsonis, identical twin brother and best friend Anastasios Tsonis and mother Isidora Tsonis. Takis leaves behind a legacy of his research on which the regeneration researchers of the future will reap benefits.

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REFERENCES

Eguchi, G., Eguchi, Y., Nakamura, K., Yadav, M. C., Millan, J. L., & Tsonis, P. A. (2011). Regenerative capacity in newts is not altered by repeated regeneration and ageing. *Nature Communications*, *2*, doi:10.1038/ncomms1389

Grogg, M. W., Call, M. K., Okamoto, M., Vergara, M. N., Del Rio-Tsonis, K., & Tsonis, P. A. (2005). BMP inhibition-driven regulation of six-3 underlies induction of newt lens regeneration. *Nature*, *438*, 858-862.

Ogura, A., Yoshida, M. A., Moritaki, T., Okuda, Y., Sese, J., Shimizu, K. K., …, & Tsonis, P. A. (2013). Loss of the six3/6 controlling pathways might have resulted in pinhole-eye evolution in Nautilus. *Scientific Reports*, *3*, doi:10.1038/srep01432

Singh, A., & Tsonis, P. A. (2010). Focus on molecules: Six3—master or apprentice? *Experimental Eye Research*, *90*(5), 535-536.

Sousounis, K., Baddour, J. A., & Tsonis, P. A. (2014). Aging and regeneration in vertebrates. *Current Topics in Developmental Biology*, *108*, 217-246.

Sousounis, K., Qi, F., Yadav, M. C., Millan, J. L., Toyama, F., Chiba, C., …, & Tsonis, P. A. (2015). A robust transcriptional program in newts undergoing multiple events of lens regeneration throughout their lifespan. *Elife*, *4*. doi:10.7554/eLife.09594

Tanaka, H. V., Ng, N. C., Yang Yu Z., Casco-Robles, M. M., Maruo, F., Tsonis, P. A., & Chiba, C. (2016). A developmentally regulated switch from stem cells to dedifferentiation for limb muscle regeneration in newts. *Nature Communications*, *7*, doi:10.1038/ncomms11069

Tsonis, P. A. (1983). Effects of carcinogens on regenerating and non-regenerating limbs in amphibia. *Anticancer Research*, *3*, 195-202.

Tsonis, P. A. (2003). *Anatomy of Gene Regulation: A Three Dimensional Structural Analysis*. Cambridge, UK: University of Cambridge Press.

Tsonis, P. A. (2007). Bridging knowledge gaps on the long road to regeneration: classical models meet stem cell manipulation and bioengineering. *Molecular Interventions*, *7*(5), 249-250.

Tsonis, P. A., & Eguchi, G. (1982). Abnormal limb regeneration without tumor production directed by carcinogens 20-methylocholanthrene and benzo(a)pyrene. *Development Growth Differentiation*, *24*, 183-190.

Tsonis, P. A., & Eguchi, G. (1983). Effects of a carcinogen N-methyl-nitro-nitrosoguanidine on blastema cells and blastema formation in newt limb regeneration. *Development Growth Differentiation*, *25*, 201-210.

Tsonis, P. A., Madhavan, M., Tancous, E. E., & Del Rio-Tsonis, K. (2004). A newt's eye view of lens regeneration. *The International Journal of Developmental Biology*, *48*(8–9), 975-980. doi:10.1387/ijdb.041867pt