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Genetic and pharmacological anti-ageing interventions

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Abstract
A remarkable recent discovery is that ageing is a malleable process and that surprisingly single mutations are sufficient to delay ageing in model organisms such as yeast, worms, flies and mice (1). These mutations that extend lifespan act by down-regulating the main cellular nutrient-sensing pathways: insulin and target-of-rapamycin signalling (1). Importantly, these long-lived mutant animals are healthier and more youthful for longer, and are also protected against a variety of age-related diseases. However, despite the well-established role of nutrient signalling pathways in ageing, the down-stream effectors are still largely unknown. There is evidence that improved protein turnover, by increased major cellular degradation pathways like autophagy and proteasome could be beneficial. Down-regulation of protein translation has positive effect on lifespan in model organisms, but the underlying mechanism is unclear (2). With life expectancy continuously increasing in modern societies, the number of people suffering from age-related diseases is rising steeply. Therefore investigation of basic mechanisms causing ageing process is expected to provide important new findings that could ameliorate health in elderly population.

In our laboratory, we use the fruit fly Drosophila melanogaster, which has already greatly contributed to the recent findings in the biology of ageing. By combining in vitro and in vivo models, as well as transcriptome and metabolome wide approaches, we hope to improve our understanding of basic mechanisms of the ageing process (3,4). We are interested in understanding how anti-ageing drugs, rapamycin and lithium, extend lifespan and if this approach is applicable to mammalian systems. I will present how up-regulation of autophagy, which is a major cellular degradation pathway, can be used to improve ageing.


Biosketch
Ivana is interested in the mechanisms of the ageing process and how we can improve ageing to prevent age-related diseases. Ivana studied molecular biology at the University of Zagreb and did a PhD at the University Pierre and Marie Curie in Paris, where she studied DNA repair pathways in E. coli under the tutelage of Dr Ivan Matic and Prof. Miroslav Radman. She then obtained an EMBO Fellowship to investigate ageing in Drosophila in the laboratory of Prof. Dame Linda Partridge at the University College London. Upon obtaining an ERC Starting Grant Ivana established her own research group at UCL Cancer Institute.