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Special issue on cancer and ageing

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An understanding of the relationship between aging and cancer is of more than mere academic interest. Biomedical research aims to intervene to prevent both. However, if the hypothesis that some aspects of the aging process itself evolved to suppress cancer is true, how will it be possible to restrain both aging and cancer?

This intellectual conundrum is intensified by the belief that cells need time to accumulate sufficient mutations for carcinogenesis to occur. Chronological time is, of course, the same for short and long-lived animals, so why is cancer a major cause of death of short-lived species like mice, as well as long-lived species such as humans (in protected environments in which death from external hazards is rare)? It seems that cancer incidence rates are governed not by chronological time but by processes that determine lifespan, at least in mammals. Thus, cancer incidence begins to rise at about the midpoint of the life span for most mammalian species. There must therefore be other explanations for why cancer rates (for most types of cancer) increase with age in both short- and long-lived animals.

These topics were discussed at a conference organised in Warsaw with the support of the European Commission, in which experts from a wide range of disciplines met to discuss the multifaceted aspects of the intriguing aging-cancer relationship. The first paper in this special issue of the Journal provides one clue to the question of why cancer rates differ in large and small rodents; Vera Gorbunova and Andrei Seluanov demonstrate an inverse relationship between telomerase activity and body size. They propose that large animals are more resistant to cancer because their somatic cells have a reduced ability to activate telomerase. Activation of telomerase is, of course, the most common mechanism by which cancer cells protect their genomes from continuous and potentially lethal erosion. Other mechanisms may also act at the “crossroads” of cancer and aging in different species. The “antagonistic pleiotropy” theory of aging may be typified by the pathway regulated by p53, as described by papers by Erica Ungewitter and Heidi Scrable, and by Renu Wadhwa and colleagues. These papers suggest that the p53 pathway may drive aging phenotypes as a

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consequence of its tumor suppressor activities. An example of a potentially practical application of knowledge gained from studies of pathways that mutually regulate cancer and aging is provided by the next paper from Ewa Sikora and colleagues. This paper describes the ability of chemotherapeutic agents to induce senescence in cancer cells, and mechanisms by which senescent cancer cells might overcome the senescence block to proliferation. The existence of common gene signatures further supports the evolutionary and molecular associations between cancer and aging, as argued in the paper by Vadim Fraifeld and colleagues. These gene signatures identify inflammation as a common driver of both aging and cancer. This commonality is supported by the identification of polymorphisms in genes encoding inflammatory factors, as argued by Calogero Caruso and colleagues. The pro-and anti-inflammatory balance in the organism may also contribute to disturbances of hematopoiesis due to the changed redox state and greater demands on the hematopoietic stem cells. Certainly, the latter are affected by aging in mice and presumably also humans, as discussed in the papers by Derrick Rossi and Luigi Warren, Daniel Pearce and Dominique Bonnet, and by Mariusz Ratajczak and colleagues.

Age-related changes affecting hematopoiesis are also likely to affect immunity and attempts to control cancer by immunotherapy. Accumulating data suggest that older individuals may respond less well than younger individuals to cancer vaccines, reviewed here by Claudia Gravekamp and Sun Hee Kim. On the other hand, certain cancer models suggest that therapeutic efficacy may increase with age, as presented here by Judith Leibovici and colleagues. It might therefore be useful to have an algorithm for assessing the “immunological fitness” of elderly people, for the purpose of estimating their ability to respond to such therapies. In the paper contributed by Katsuiki Hirokawa and colleagues, such a system is proposed for clinical use. Measuring the impact of such therapies requires the availability of biomarkers for the presence of cancer cells; N-glycan profiling may offer a simple, non-invasive novel technique for this purpose, as proposed by Chitty Chen and colleagues. Finally, epidemiological issues considered by Anatoli Yashin and colleagues suggest that the impact on longevity of controlling cancer may be much greater than currently appreciated if cancer deaths are considered independently of other causes of death. This is because there are negative correlations between the occurrence of cancer and certain other diseases. Possibly, this negative correlation could be due to systemic changes that cause and are caused by carcinogenesis, as argued in the contribution by Vladimir Anisimov. This paper highlights changes to the immune and endocrine systems, which will greatly affect health and aging trajectories, independent of the disease of cancer itself. The last paper in this special issue, by Evgeny Imyanitov, further discusses the intriguing possibility that many of the pathways and mechanisms that increase cancer risk nonetheless contribute to increased longevity due to their “anti-ageing” actions. Enhancing these latter pathways might thus enhance healthy longevity, provided that any “side effects” of increased cancer incidence could be controlled by other therapies, for example immunotherapy. This exciting meeting initiated many rigorous discussions which will undoubtedly continue until the problems of both cancer and aging have been finally resolved.