Philip Savage, J Cancer Sci Ther 2017, 9:5(Suppl)
DOI: 10.4172/1948-5956-C1-102

Chemotherapy curable malignancies; Unique genetic events, frozen development, natural apoptosis and absent cancer stem cells

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Despite over 40 years of the 'War on Cancer' the list of metastatic malignancies that can be cured with drugs is unchanged from the 1970s. Whilst the paradigm of cancer cells being sensitive to DNA damaging chemotherapy as a result of rapid growth and then developing chemotherapy resistance and hence avoiding being killed is well established. We would like to present an alternate interpretation of the data and a new hypothesis. The new hypothesis relates to the biological properties of the chemotherapy curable cancers which comprise trophoblast tumours, germ cell tumours, acute leukemia, high grade lymphoma, and the rare childhood malignancies. Each of the chemotherapy curable malignancies arises from specialist cells that naturally undergo DNA manipulations that are intrinsically associated with high levels of endogenous apoptosis during development. Trophoblast tumours arise from the cells of conception, which have just undergone nuclear fusion. Germ cell tumours arise from pre-malignant precursor cells that are subject to pressures to undergo meiosis and mitosis. In the B cell malignancies, acute leukaemia that arises from cells linked to VDJ rearrangement of the immunoglobulin genes, whilst diffuse large B cell lymphoma which is closely linked to somatic hypermutation. Each of these unique genetic processes is naturally linked to a period of extreme sensitivity to DNA damage/apoptosis and we would argue that this apoptotic sensitivity is then maintained in the malignant cells arising at these developmental points. The other key biological characteristic the chemotherapy curable malignancies have is that their unusual developmental pathway means that they are not linked to any conventional hierarchical cancer stem cells. As a result, there is no pool of chemotherapy resistant stem cells available to replenish the tumour after treatment. Further pathway based research may be interesting and lead to novel therapeutic avenues.

Biography

Philip Savage is a Consultant Medical Oncologist in Brighton, UK. His Medical degree is from Bristol University and trained in Medical Oncology at the Royal Marsden and Hammersmith Hospitals in London. He previously specialised in the treatment of trophoblast and germ cell tumours whilst working at Charing Cross Hospital in London. He holds a PhD in tumour immunology from London University and has additional research interests in healthy economics and cancer treatment history.

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