**Molecular mechanism of malignant change by Benzopyrene-induced cellular senescence**

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**Introduction.** The association between chemical substances like benzopyrene (BP) and cancer has been extensively studied for years. However, the majority of research has cantered on the initial stages of carcinogenesis, which occur early in cancer development. Understanding the malignant change process that leads to cancer recurrence and metastasis still lacks comprehensive insight. In this point, recent discoveries have revealed that BP induces cellular senescence, a state of growth arrest triggered by cellular stressors such as DNA damage, which has been implicated in malignant change.

**Aims**. Our study seeks to uncover how BP contributes to malignant change by inducing cellular senescence.

**Methods**. Exposure of estrogen receptor (ER)-positive breast cancer cells MCF7 to BP or benzopyrene diol epoxide (BPDE) (0, 0.1, 1 µM) for 3 days induced cellular senescence. Additionally, RNA-seq analysis was conducted on MCF7 cells induced with cellular senescence by BP and BPDE, aiming to identify potential candidate genes contributing to malignant change.

**Results.** Cellular senescence was induced in MCF7 cells following a 3 days exposure to BP and BPDE. Following BP exposure, MCF7 cells initially displayed reduced cell proliferation akin to typical cellular senescence. However, continued cultivation in BP-free medium led to the restoration of proliferation capacity, ultimately indicating the potential for acquiring even greater proliferation ability than prior to BP exposure. Mechanistically, exposure to BP resulted in the nuclear translocation of Aryl hydrocarbon receptor (AhR) and ERα prior to changes in cellular senescence markers being observed. Furthermore, RNA-seq analysis revealed a downregulation of several genes commonly associated with the suppression of cancer malignant transformation in both BP and BPDE exposure groups.

**Discussion.** BP was suggested to induce cellular senescence. Furthermore, the senescence induced by BP indicated the potential for reversible recovery of cell proliferation ability. Our future efforts will focus on elucidating the mechanistic link between AhR and the candidate genes identified through RNA-seq analysis.