Cancer mutations in normal tissues

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Cancer is a clonal disorder derived from a single ancestor cell. However, the presence of a clone does not necessarily mean cancer. On the contrary, it has become more and more clear that expansion of positively selected clones in physiologically normal/non-cancerous tissues is commonly seen in association with normal ageing and/or in response to environmental insults and chronic inflammation. Recent studies have reported expansion of driver-mutated clones in blood, skin, oesophagus, bronchus, liver, and endometrium, where the expansion could be so extensive to remodel almost entire tissues. A conspicuous overlap between driver genes in cancer and normal tissues suggests a strong link to cancer development, providing an important clue to understand early carcinogenic processes. Nevertheless, the presence of drivers that are unique to either cancer or normal tissues indicates that these clones may not necessarily be destined for cancer, but even negatively selected for carcinogenesis depending on the mutated drivers. Moreover, tissues that are remodelled by genetically altered clones might define functionalities of aged tissues or modified inflammatory processes. In this meeting, focusing on clonal expansion in the esophagus in aged people and in the colon exposed to chronic inflammation, I will discuss how positive selection occurs in normal and cancer tissues.