



## Tumor Heterogeneity and Its Clinical Significance

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### Editorial

The tumor of human body, especially malignant tumor, is composed of cells with different pathological and biological behavior. The heterogeneity of tumor mainly refers to the difference of tumor cells in the same tumor due to different tumor cell line. The heterogeneity of tumors was first discovered in histology, and later extended to hormone receptor, metabolism, growth rate and sensitivity to chemical drugs. The internal structure of the tumor is very complex. It has been proved that there were differences in invasion and metastasis of malignant tumor cells, and metastatic potential between different cell subsets. The tumor cells in the primary infiltrating area were more similar to those of the tumor to the surrounding cells. The tumor microenvironment refers to the tumor internal oxygen supply, acidity, nutrient supply. The tumor microenvironment in a region may be beneficial to the growth and proliferation of the tumor, while the other region is relatively unfavorable to the growth and proliferation of the tumor.

Since the entire arrangement inside tumor (heterogeneity) is uniformity, whether treatment and prognosis can represent the precise tumor entity, whether it contains the cells with the most invasive ability which pathology examination can accurately judge the prognosis.

### Heterogeneity of histological appearance

Some research found that in carcinoma of gingival, tongue and oropharyngeal cancer, deep infiltrating cancer cells usually cell differentiated poorer than in the superficial part of the lesion. Bryne et al once reported that the cells of the infiltrating region of Oral Squamous Cell Carcinoma (OSCC) had a lower degree of differentiation compared with the central area.

More attention is now paid to the deeper invasion part of the malignant tumor, especially at the junction between the tumor and the normal tissue. The depth of tumor invasion is an ideal area to study the mutual interaction of the tumor and the host. It could best reflect the characteristics of the current stage of the tumor, and it of important significance for the choice of treatment and prognosis judgement.

### Heterogeneity of microenvironment especially angiogenesis

The microenvironment of the tumor, the microenvironment of the target organ and the genetic background of the host, also have a complex heterogeneity, which has a great impact on the development of tumor metastasis potential.

Angiogenesis is a prerequisite for tumor growth, is closely related with tumor growth, it not only provide nutrients for growth and proliferation of tumor angiogenesis, and increased tumor cells into the vascular opportunity, can promote the metastasis of tumor cells. It was reported that patients with lymph node metastasis had more obvious vascular invasion, and the 5 year survival rate was significantly lower. There is no doubt that the study of vascular morphology and function is of great significance to the understanding of the biological behavior of tumor, the choice of treatment and the prognosis. In recent years, great progress has been made in this field, but there are only a few reports about the differences between the different regions of angiogenesis.

### Heterogeneity of molecular biology

Riviere A et al found that the expression level of C-myc in the deep infiltrating area was higher than that of the tumor surface in the squamous cell carcinoma of the oral and maxillofacial region and the vulva.

Proliferating Cell Nuclear Antigen (PCNA) is a marker of tumor proliferative activity. Immunohistochemical study found that PCNA positive cells of well-differentiated laryngeal carcinoma is mainly distributed in the basal layer, but in poorly-differentiated laryngeal carcinoma it were scattered or patchy distribution. This may be due to poor differentiation, more invasive and

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metastatic potential of tumor cells in the presence of deep infiltration zone.

The concept of multiple factors and multiple genes involved in tumor has been widely accepted. Tumor heterogeneity that tumors are not from the single tumor cells evolved, in different stages, there

are new different genes involved, it may exhibit different biological entity. In the study of the tumor, the observed manifestations may not reflect the characteristics of the current stage of the tumor. The heterogeneity of malignant tumors may be of great significance in the diagnosis, treatment and prognosis of tumors.