

Cancer Cell Nucleus: An Insight

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Introduction

Nucleus reflects a cell's biological potential and activity. Nuclei of normal healthy cells are usually single per cell in number, round to oval shaped, show even distribution of chromatin, display regular nuclear margin or membrane, one or two inconspicuous nucleoli and normal mitotic figures. During development of cancer, the nucleus undergoes numerous alterations of size, shape, number, nuclear membrane or margin, chromatin pattern, nucleoli, and organization of nuclear chromatin.

Nuclear Area and Perimeter

Rapid and abnormal proliferation of tumor cells results in increased nuclear area and perimeter (Figures 1-3). Studies in different types of cancers have shown that the nuclear area and perimeter increase gradually with increasing grades of carcinoma [1-4].

Nuclear Shape

In cancer, nuclei can become irregular or elliptical with coarse heterochromatin aggregates (Figures 3 and 4) [4]. Increased fragmentation or budding of nuclei, ring-shaped nuclei, and nuclear holes are often noted in cancer nuclei as well [5]. Profound anisonucleosis is evident in high grade tumors [4,6].

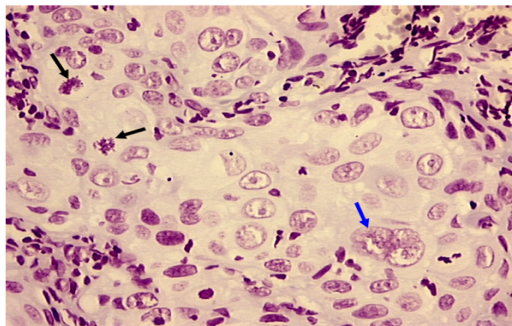


Figure 1: Photomicrograph of oral squamous cell carcinoma showing enlarged, elliptical tumor nucleus with prominent nucleoli, uneven membrane, (blue arrow) and bizarre mitotic figures (black arrows). Objective 20x, Feulgen stain.

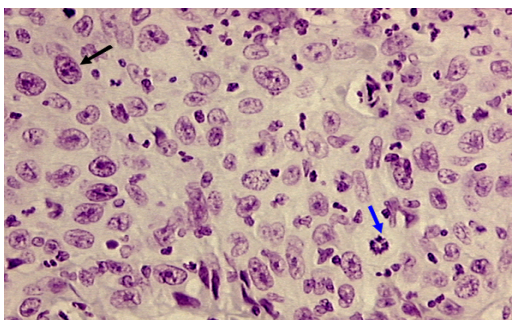


Figure 2: Photomicrograph of oral squamous cell carcinoma showing tumor nucleus with multiple prominent nucleoli (black arrow) and bizarre mitotic figure (blue arrow). Objective 20x, Feulgen stain.

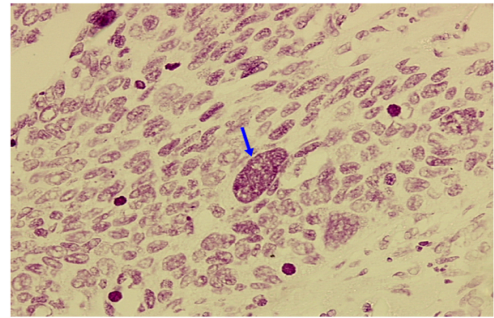


Figure 3: Photomicrograph of poorly differentiated oral squamous cell carcinoma showing profound anisonucleosis and large tumor nucleus with chromatin clumps (blue arrow). Objective 20x, Feulgen stain.

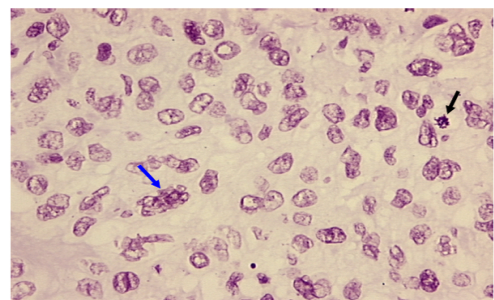


Figure 4: Photomicrograph of oral squamous cell carcinoma showing tumor nucleus with multiple nucleoli, irregular nuclear membrane (blue arrow) and bizarre mitosis (black arrow). Objective 20x, Feulgen stain.

Nuclear Number

Multinucleation is also commonly observed feature in malignancy [4]. The presence of micronuclei is also known to correlate with the grades of carcinoma. Disturbed mitosis, separation of a fragment or entire chromosome from the bulk of DNA results in formation of micronuclei [5].

Nucleoli

Nucleoli are usually inconspicuous in normal cells while nucleoli become prominent, more in number, enlarged and irregular with occasional sharp pointed projections in malignant cells (Figures 1, 2, and 4) [4]. The number, size and irregularity of nucleoli increase with increasing

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grades of carcinoma [4,6-9] and is related with the aggressiveness of the tumor; it can be used to assess the clinical outcome [9].

Nuclear Chromatin

The finely granular chromatin of the normal cell transforms into irregular clumps with variable size, shapes and sharp pointed projections (adhesion of abnormal chromatin clumps to the inner surface) in the neoplastic cell (Figures 3) [4]. Sometimes, a salt-and-pepper chromatin, opened up reticular chromatin, irregular coarse clumped chromatin, and vesicular chromatin may also be observed [6]. The possible factors responsible for change of chromatin pattern are chromatin relocation, chromatin remodeling, DNA aneuploidy, change of nuclear matrix protein, and change of nuclear pore [6].

Nuclear Membrane

Irregularity of membrane has been shown to increase with increasing grades of carcinoma (Figure 4) [4]. It may be seen as nuclear grooving, nuclear molding, and nuclear convolutions or irregular thickening of nuclear margin [6].

Mitotic Figures

Mitotic figures are characterized by an absent nuclear membrane with clear, hairy extension of nuclear material (condensed chromosomes) either clumped (beginning metaphase), in a plane (metaphase/anaphase), or in separate chromosomal aggregates (anaphase/telophase). Normal mitoses are observed in rapidly proliferating tissues. However, abnormal or bizarre mitoses are seen in malignancy (Figure 1,2 and 4) [4]. Higher grades of carcinoma show frequent abnormal mitotic figures than lower grades of carcinoma [4,7].

Detection

Nuclear changes can be studied using microscopically stains like Haematoxylin and Eosin, Feulgen stain, Papanicolaou stain, Giemsa, or Romanowski stains. Nuclear morphometry is helpful to characterize the size and shape of organelles and structures, such as nuclei, nucleoli, nuclear membranes, and chromatin granules and has been used for

grading various carcinomas and also to differentiate metastatic from non-metastatic tumors [3].

Conclusion

Advanced molecular techniques like immunohistochemistry, flow cytometry [5] and interphase fluorescent *in-situ* hybridization are now available to localize and quantify specific DNA sequences or proteins. The newer technologies to observe the gene expression and simultaneously nuclear structural changes may provide fresh insights into the architectural organization in cancer nuclei. This may help to develop various cancer-specific biomarkers and cancer-specific drug targeting.

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