Part I
Cancer

1 Causes

1.1 Cell Cycle Regulation by Checkpoints

The mitosis system evolved to have checkpoints in place to monitor and regulate the fidelity of cell functioning. This includes but is not limited to:

- growth to appropriate size
- replication and integrity of chromosomes
- proper segregation of genetic material during mitosis

Many of these safeguards are ancient in origin and can be observed in primitive organisms such as yeast. There also exist checks which have evolved especially in organisms with more complex tissues differentiation. Many of these checkpoints have significant impact on tumor suppression [2]. Additional exploration here is both interesting and could worth while but remains beyond the scope of this document.

Cancer is the uncontrolled and rapid division of cells. The mass of cancer cells forms tumors. The rapid and unchecked division of cells leads to further mutation which can cause cells to leave their primary sites and form satellite tumors in a process called metastasis.

1.2 Cancer Genetics

Mutations which take place on genes that control cell division directly are called Oncogenes and lead to uncontrolled proliferation.

There are also genes that act as tumor suppressors, these are often recessive and both copies of the genes need to be effected in order to cause the uncontrolled proliferation.

1.3 Gene p53

Gene p53 which codes for a protein that acts as a transcription regulator that attaches to DNA and turns gene expression on. It plays a role in tumor suppression, DNA damage repair, triggers cell division and initiating cell growth [3].

The amino acids located at the center of the p53 protein controls its ability to regulate transcription of genes necessary for either cell division or cell death according to the organisms needs. It is mutations of the gene of the p53 protein is a well researched path in which eventually lead to cancer formations via uncontrolled transcription genes controlling cell proliferation.

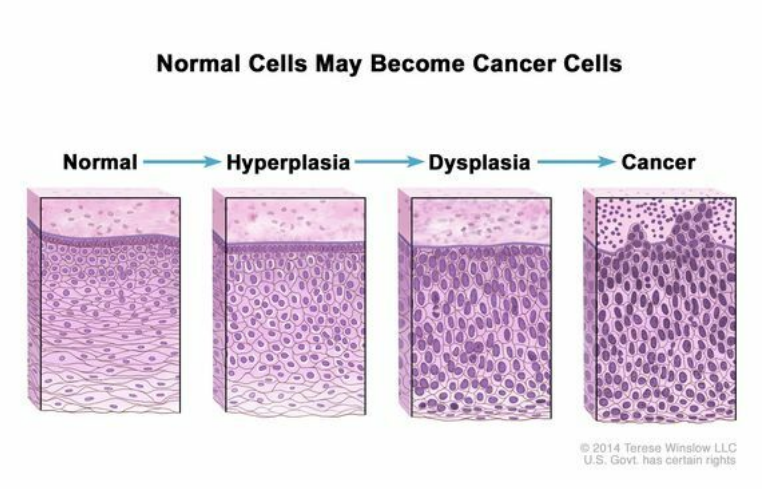

Figure 1: Illustration showing the progression of classification types between normal cells and cancer [1].

2 Diagnosis

2.1 Histology

Cell arrangements in a tissue can be categorized in a number of ways on the spectrum between healthy tissue to tumor formation:

- Normal
- Hyperplasia - increase in the number of cells in the tissue while still appearing normal under a microscope.
- Neoplasia - uncontrolled hyperplasia
- Dysplasia - cells begin to appear abnormal but are not yet cancer.
- Cancer

An illustration can be found in figure 1.

2.1.1 Responses to Neoplasia

There a three main tissue responses to neoplasia:

- Desmoplasia: A stromal response as a reactive formation of connective tissue
- Inflammatory response: inflammatory cells rush in.
- Vasucular: angiogenis of new blood cells - hard to tell in slide

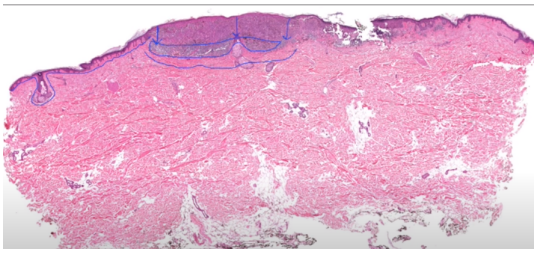

Figure 2: The left image shows an example of an invading epithelial cancer. The circled blue region in the middle of the slide, just below the drawn arrows, shows a thick collection of inflammatory cells. Above that is an extremely thick hyperplasia of epithelium. The basement membrane, which remained fully intact to the left of the inflamed region, appears to be fully broken down in the highlighted area and marks a region of desmoplasia.

Figure 2 shows an image taken by a light microscope where the desmoplasia and the inflammatory response can be clearly seen as well as a rupture of the basement membrane.

2.1.2 Basement Membrane

The basement membrane is an important structural feature when talking about epithelial cell histology. It acts as a structural support for epithelial cells and which forms a separation between tissues.

The basement layer describes what is seen while using a light microscope and the basal lamina and the reticular lamina, two separate parts of the basement layer, can be seen using an electron microscope.

Cancers will uncontrollably replicate and push against the basement membrane until the developing tumor finally ruptures through it. The three physiological responses mentioned above are meant to prevent and prepare for that moment.

2.2 Diagnosis from a zoomed in sample

2.2.1 The ABCDE of diagnosis

- Anapalesia - cells don't follow regular tissue organization.
- Bizarre - cells are not uniform and irregular in shape and size, large cells are generally the cancerous ones.
- Chromatin - extra chromatin, darker than usual cells.
- Displasia - displaced growth.
- Edges - well defined or messy edges. The messy edges point to cancer.

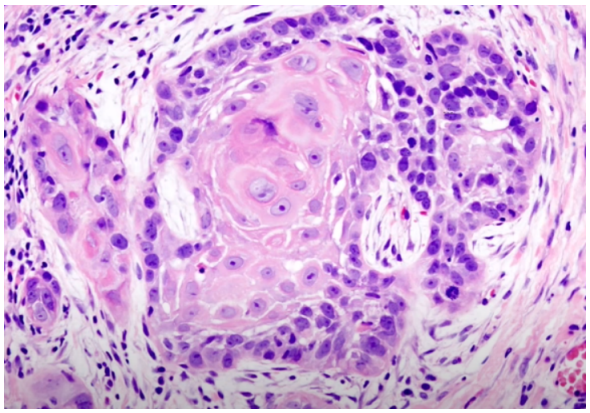

Figure 3: This image of oral cancer shows the bizarre irregularities of shape and size often found in cancers. Not the large and multi nucleated cells in the middle to the small cells surrounding them. The chromatin is seen to mare a separation between the cells. Also note the surrounding nearly white desmoplasia around the cancer cells, bordering the sides.

Figure 3 shows oral cancer displaying many of the tell tale signs of cancer.

Sometimes we could have many of these markers without the basement membrane being broken - in such cases the slides would be categorized a dysplasic and not cancerous.

References

[1] Definition of dysplasia - NCI Dictionary of Cancer Terms - NCI, February 2011. Archive Location: nciglobal,ncienterprise.

[2] Kevin J. Barnum and Matthew J. OConnell. Cell Cycle Regulation by Checkpoints. *Methods in molecular biology (Clifton, N.J.)*, 1170:29–40, 2014.

[3] Xin Lu. 9 - p53: A Target and a Biomarker of Cancer Therapy? In Xin-Yuan Liu, Sidney Pestka, and Yu-Fang Shi, editors, *Recent Advances in Cancer Research and Therapy*, pages 197–213. Elsevier, Oxford, January 2012.