Cancer diary of osteosarcoma

Life

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My name is osteosarcoma. I am highly malignant tumor of mesenchymal origin and the second most common primary malignant bone tumor . I am originate from mesenchymal cells. I have spindle shape and hyper chromatic nucleus. I have been formed when osteoblasts cells secreted malignant osteoid.

I am like osteoblast (bone forming) cells, but I cannot make strong matrix like them. You know that osteoblasts originate from immature mesenchymal stem cells. So my ancestors are from those. But I am already modified in to osteosarcoma cell. I can occur at any bones found in the body. I am more frequent at sites of the most rapid bone growth; those are extremities of long bones near metaphyseal growth plates.

From the sites that I frequently choose ; distal and proximal end of femur (42%), proximal end of tibia(19%), proximal end of humerus (10%), pelvis skull and jaw(85%) and pelvis(8%). I can be appearing 1 to 3 million people per year. Off course, I am rare compared to other types of cancer. I can attack any age as primary osteosarcoma but mostly between 10-25yrs. I can also come at older individuals as secondary osteosarcoma. I affect males little bit more than females.

I am most common in patients with Fraumeni syndrome, Rothmund-Thomson syndrome, Bloom and Werner syndromes. Exposing to Paget disease and

ionizing radiation give favorable conditions for me to develop our colony. Fig 1. Osteosarcoma genesis and osteogenesis When I was changing to osteosarcoma, there was a mutations of MDM2 amplifications which led to p53 gene inactivation. Another controller gen which is called retinoblastoma (RB) genes was also altered.

I become safe because there is no more check point and control for me . But the normal bone cells have several check points in their cell cycle. In the presence of RB mutations I will occur at an incidence 500 times that of the normal population. Normal cells are always worrying for G1/S check point but I am not, because the p53 and Rb genes are already mutated (lost their function). I am preparing more DNA and for that I am also synthesizing mRNA and important proteins.

During my replication time I gained chromosome number 1 and lost chromosome 9, 10 and 13. Till now I am successfully dividing and I am forming other similar cells. In near future I will have my own colony of cells and my own sarcoma tissues01//14/2014As usual I was preparing to divide but the proteins detected a damage in my DNA. The damage was too big to be repaired. Even if it is bigger damage I will not go to programmed cell death called apoptosis.

Because this is not my character. My only goal is to survive and proliferate more. This is my unique behavior. Of course I was not like this, I was following the normal path of cell cycle and programed cell death. This thing happened after I lost my DNA sequence that triggers cell death pathway. 5/18/15Recently I got another mutations and my FOS and Jun proteins are up

regulated. Those proteins are components of activator protein1 complex (AP-1).

AP-1 his regulator of cell transcription. Now I am getting additional energy because my transcription regulators are out of service. I can proliferate freely and destroy bone cortex and extend towards bone marrow cavity and soon out wards towards adjacent soft tissues. 10/17/15I am now thinking why not I visit other organs. I have information lung, liver and also other bones are the safe place and more fertile to me .

When I become more organize, I can migrate and live there. I am already resistant to programed cell death (anoikis) and can exhibit anchorage independent growth (AIG). Abnormal integrin? ?? v6, Rho, ATPase e. g. Racl and Cdc42 upregulated p13 kinases which in turn inhibited proapoptotic factor Bad and this protected me from apoptosis even when I am not attached to any membrane. Now I have bigger size with hypoxic and acidicenvironment. So I need supporting blood vessels to obtain oxygen and nutrients I have done angiogenesis for my sustained growth and further metastasis.

My intrinsic conditions have to lead to stimulation of von Hippie Lindau protein. It releases hypoxia inducible factor-1? (HIF-?)which further up regulates several VEGF gene such as VEGF A through VEGF E. This further releases Nitric oxide (NO) from endothelial cells and results in vasodilation and increased vascular permeability. By doing those processes I got leaky and irregular vasculature. 3/14/16 I am starting flight to lung.

I am using integrin proteins, which found in my surface , in attaching to matrix proteins (fibronectin). For my signal transduction and interaction with other cells, I use integrin along with ezrin protein , foal adhesion kinase (FAK), protein kinase C (PKC) and Rho GTPase. They also help me for my conformational changes. Besides to this matrix metalloproteinase (MMPs) are helping me in my sojourn through blood vessels and tissue renewal process.

Now I have reached the lungs and I am growing, multiplying and consuming all nutrients. It is like as I heard . I like it. 10/10/2016Today, the patient could not resist me . He took me to hospital. Because I create sever pain and swelling. I was diagnosed by radiograph as high grade sarcoma. Additionally they did CT scan, RI and biopsy and confirmed my stage. They are now discussing to fight against me. Yes they have started chemotherapy (high dose methotrexate, doxorubicin and cisplatin).

I have been fighting against those drugs for the last three months and I am now getting old, starving and feeling weaker day by day. Oh those drugs become treble for me. Methotrexate is a dihydrofolate reductase inhibitor, it can block folic acid supply which is needed for my RNA and DNA synthesis. Doxorubicin which is also a drug that interact with my DNA and inhibits biosynthesis of macro molecules. Cisplatin causes damage to my DNA. I have to create solutions, because I am no longer able to make RNA efficiently. But I am struggling to continue my life.

I got another mutations which is alteration in reduced folate reductase (RFC) protein Leu291pro. Yes I did it. This alteration unable carrier to transport methotrexate towards me . Besides to this, membrane pump-glycoproteins

(P-gp) is also helping me with pumping out these drugs. Due to this I start dividing and spreading slowly but steadily. Other worse situations are happening to me, they are using high energy rays (x-rays) to kill me. I am no longer able to grow. I am shrinking.

4/14/18The worst thing are happened on me. Now, they are performing surgery and removing me as cancerous tissue. I was sending my daughters to afar to lung. By myself I am highly depressed and weak due to huge loss my colony. I try to grow and spread again by my reserve soldiers and by those immigrant members.

They are still in dilemma to administer chemotherapeutic agent after surgery. The people are always struggling to combat me and other friends. If they post-surgery chemotherapy no more survival . I say good bye I will not be there anymore.

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