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Using the Electromagnetics of Cancer's Centrosome Clusters to Attract Therapeutic Nanoparticles

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Abstract

This paper summarizes recent research findings concerning centrioles, centriole duplication, centriole overduplication, supernumerary centrioles, centrosomes, and centrosome amplification. The paper then discusses the status of ongoing research on the use of nanoparticles for cancer treatment. The research findings show that a centriole produces an electromagnetic field apparently due to the longitudinal oscillation of its microtubules (MTs). A cluster of centrioles is therefore presumed to produce an enhanced electromagnetic field. Individual centrioles are immersed in a cloud of electron-dense material (proteins) which together with the centrioles is known as the centrosome. A cluster of centrioles thus produces a cluster of centrosomes—a hallmark of cancer cells. With enhanced electromagnetic fields, centrosome clusters provide an attraction for magnetically charged nanoparticles. These nanoparticles however are not attracted to normal cells which with only two (or at most four) centrioles, have a weaker magnetic field. The idea is simple: Magnetized and therapeutic nanoparticles are directed toward tumors and then attracted to the centrosome clusters of the tumor cells. Once inside the tumor cells, the nanoparticles can release their toxins.

Keywords

Centrioles, Supernumerary Centrioles, Cell Electromagnetism, Theraputic Nanoparticles, Tumorigenesis, Cancer

1. Introduction

The recent widespread use of electron microscopy, and currently the use of atomic force measurements, in

studying internal cellular structures have provided an improved understanding of the geometry, composition, and functioning of the centrosome, the centrioles, and the microtubules. Many questions still remain. But based on the findings to date, the imagings show that within a cell, adjacent to the nucleus, is a pair of tiny organelles (approximately 400 nm in major dimension) known as "centrioles". The centrioles may be viewed as a pair of annular cylinders perpendicular to each other at the cylinder bases. The cylinders themselves are composed of nine blades of microtubule triplets as represented in **Figures 1-3** [1] [2].

The centrioles are the principal drivers of cell division (mitosis). They lead the mitosis by first duplicating themselves so that there are then two pairs of centrioles—a "mother" and a "daughter" pair. The daughter centriole then separates from the mother and moves around the nucleus to the opposite side.

At the same time the nucleus membrane softens so that the nucleus can be pulled apart by the mother and daughter centrioles on the opposite sides. Also, at the same time the DNA within the nucleus is being copied (duplicated) and separated with one part going with the mother centriole side of the nucleus and the other with

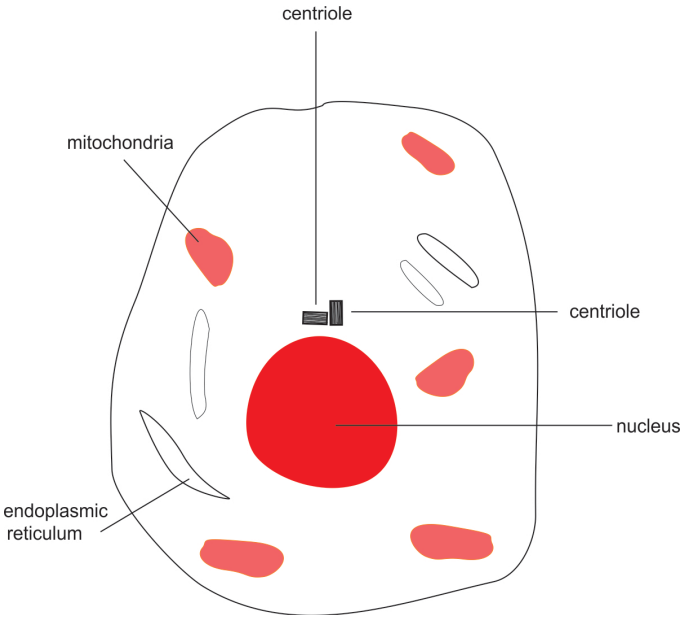

Figure 1. Cross-section of a typical eukaryotic (animal/human) cell.

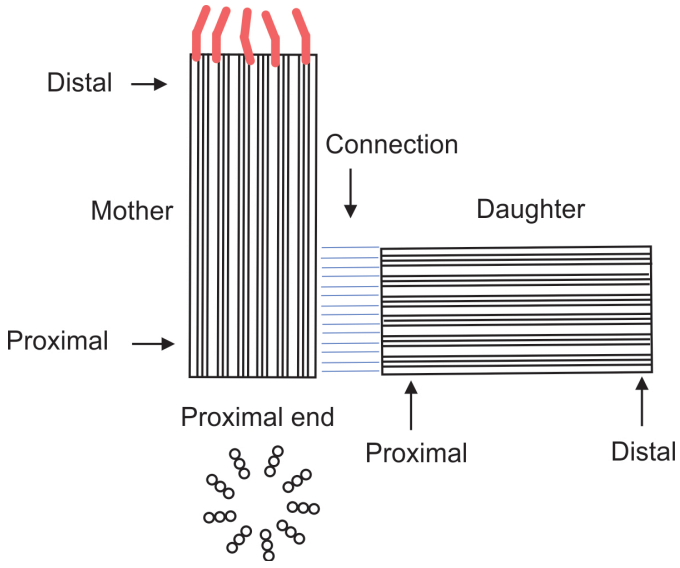

Figure 2. A centriole pair.

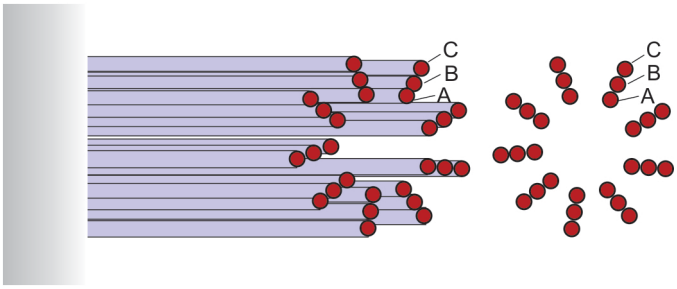

Figure 3. Microtubule blades of a centriole.

the daughter side.

As the mitosis continues, the remainder of the original cell's cytoplasm with its organelles is divided between the separating parts and then two new cells emerge.

Mechanically this activity can be regarded as due to forces exerted at a distance, as opposed to forces exerted by contact. Such distance exerted forces are characteristic of electromagnetic forces.

When this process goes awry the cell either dies or it becomes malignant. The malignancies arise by a failure of the centrioles to duplicate once and only once, but instead several centrioles are produced during the duplication. That is, a "mother centriole" produces more than one daughter. When this happens, the DNA copying is also disturbed leading to chromosome instability.

The overduplication of the centrioles then leads to supernumerary centrioles which in turn stimulate rapidly developing cell separation and then a tumor of malignant cells.

To see how this can happen consider that when there are supernumerary centrioles within a cell the centrioles tend to coalesce with each centriole pair bringing with it a surrounding cloud of electron dense proteins. This coalescence results in a cluster of centrioles and centrosomes or "centrosome amplification".

Recent studies show that most, if not all cancerous tumors have supernumerary centrioles [3]-[40]. Excessive centrioles frequently gather together leading to the formation of centrosomal clusters.

With mitosis beginning with centriole duplication, supernumerary centrioles accelerate the rate of cell division, and in the process cause aneuploidy in the nucleus and chromosome instability (CIN).

Recent studies also show that the centrioles via their vibrating microtubules (MTs) develop an electromagnetic field within the cell [41]-[66]. Therefore, if there are supernumerary clustered centrioles, the overall electropolarity of the cell is believed to be enhanced.

Also in recent years, with the ongoing advances of nanotechnology, nanoparticles have been developed which are sufficiently small that they can penetrate cell membranes [65]-[80]. Consequently if the nanoparticles are magnetically charged, they could be attracted by the presumed magnetic field surrounding the clustered centrioles. If the nanoparticles adhere to the centrosomal cluster, toxins and/or heating can be externally released and/or induced to destroy the cell.

Normal cells with only one pair of centrioles, and thus lower electropolarity of cancer cells, will not be an attraction for the magnetically charged nanoparticles.

The following paragraphs provide additional detail, and a basis for the foregoing assertions. Reference [1] provides additional background information.

2. Centrioles and Electromagnetism

To see how centrioles with their vibrating microtubules can establish an electromagnetic field of a cell, recall first some of the unique features of these organelles.

1) Centrioles occur as a pair of small orthogonal cylinders lying adjacent to the nucleus. See **Figure 1**.

2) Centrioles have precise and uniform geometry, being approximately 400 to 500 nanometers (nm) long and approximately 200 nm in diameter. See **Figure 2**.

3) Unlike all other organelles and organs, centrioles have no membrane cover.

4) Instead, centrioles are hollow cylinders with a perimeter of nine radially inclined "blades" of microtubule (MT) triplets—as represented in **Figure 2**.

5) As with DNA, centrioles are self duplicating.

6) Finally, and of greatest importance for our consideration, centrioles are the principal drivers of mitosis-from initiation through division.

Next, although centrioles occur in pairs with precise geometry, they are not identical. One (the "daughter") is a bit shorter, and interestingly, it is attached to the side at the end (or base) of the other (the "mother") as in **Figure 3**. This intersection is considered to be at the "proximal" end of the centrioles. The intersection itself is immersed in a cloud of electron dense pericentriolar matter known as the "microtubule organizing center" (MTOC).

The centrioles together with the MTOC are known as the "centrosome".

With the high electron density of the MTOC, the electropolarity of the proximal centriole ends is taken as "negative" with the distal ends then being "positive".

In more focused detail, the microtubules (MT) in the centriole blades are themselves hollow cylinders, but with varying lengths (approximately 400 to 500 nm) depending upon the overall centriole length. The MT inside and outside diameters are approximately 15 and 25 nm. The MT cylinder walls are composed of 13 tubulin filaments evenly spaced around the circumference and running lengthwise along the cylinder, as represented in **Figure 4**.

The MT filaments are composed of α and β-tubulin dimers laid end-to-end as in **Figure 4**. These filaments have smooth surfaces, allowing them to slide longitudinally. The tubulin dimers have ionic polarity with again the proximal end being negative and the distal end being positive.

The longitudinal movement of the MT filaments is oscillatory with a frequency of approximately 465 MHz [81]. It is this vibration that is believed to give rise to the electropolarity of the centriole and thus also to the cell itself.

3. Electro-Polarity of Dividing Cells and Cancer Cells

When a cell is about to divide the centrioles begin to duplicate by growing new "daughter") centrioles on their sides at their adjoining bases which are emersed in the electron dense cloud of the MTOC. The nascent centriole appears to arise when a small deposit of the protein Plk4 (aka "SAK") is placed on the outer MT of the "mother centriole" [82] (see also [22] and [83]-[91]). The nine-fold cartwheel geometry of the MTs is then developed by the protein SAS-6 joined to the small SAK deposit [22] [84] [86] [87] [89]-[92].

Once the MTs of the daughter centrioles become mature and begin to oscillate they enhance the overall electromagnetic field of the (now four) centrioles. That is, once the pair of centrioles becomes two pair the intensity of the electromagnetic field is potentially doubled.

Suppose now that there is an error in the centriole duplication where the mother centriole has two or more

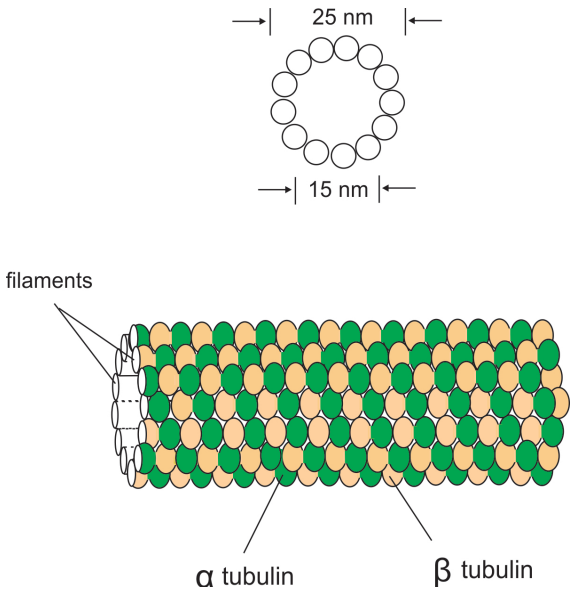

Figure 4. A microtubule (MT).

daughter centrioles. Suppose further that this defect of overduplication persists so that there are numerous centrioles, or "supernumerary" centrioles within the cell. Suppose still further that due to electromagnetic field interactions these multiple centrioles cluster together as is characteristic of cancer cells [14] [21] [26] [28] [40] [88] [93]-[100]. Then the resulting electromagnetic field of the cluster is presumed to be many times greater than that of a single centriole pair.

For some cancerous tumors, specifically breast cancers, this increase in electromagnetism can even be measured at the breast surface [59] [62].

4. Application of Nanotechnology

The modern era of nanotechnology began about 1995 with an emphasis upon micro-manufacturing. More recently applications have been expanding including a focus upon biosystems.

"Nano" normally refers to dimensions of the order of 10^{-9} m. That is, 1 nanometer (nm) equates to 10^{-9} meters (m). A "nanoparticle" is thus one with nano-size dimension—that is, with major dimension d being: $1\text{ nm} \le d \le 100\text{ nm}$.

With the characteristic dimension of a cell being approximately 10 to 30 μm it is easy to visualize nanoparticles being able to penetrate a cellular surface.

In recent years many investigators have envisioned the use of therapeutic nanoparticles to treat malignant tumors. The idea is simple: If a nanoparticle can penetrate a cancer cell and release a toxin, while at the same time avoiding normal cells, an effective new cancer treatment will have been attained.

Here are a few quotes:

"Nanomedicines have enormous potential to improve the provision of cancer therapy, yet our ability to efficiently home these materials to regions of disease *in vivo* remains very limited".

---G. von Maltzahn *et al*. [78]

"Within the family of nanomaterials, carbon nanotubes (CNT) have emerged as a new alternative and efficient tool for transporting and translocating therapeutic molecules".

---A. Bianco *et al*. [100]

"To date, nanoparticles represent the most widely used carrier system for multifunctional drug delivery applications".

---F. Wang *et al*. [73]

In spite of this optimism, the major problem is still how to effectively get the therapeutic nanoparticles into the cancer cells. D. Shi *et al*. [74] have suggested using magnetically charged nanoparticles and external magnetic fields to guide the particles to the tumors.

To carry this further, the way to have the therapeutic nanoparticles focus upon the cancer cells and yet avoid harming normal cells is to take advantage of the differences between cancer and normal cells, and specifically in this research, the differences in the electromagnetic properties of cancer and normal cells.

Advances in nanomaterials technology, and particularly in carbon nanotube technology [100], are enabling the sensitizing and charging of nanoparticles to make them attracted to electromagnetic sources, and specifically with centrosome clusters.

5. Discussion

With some effective chemotherapies slowing the development of centrosome amplification, it follows that destruction of centrosome clusters will be an even more effective therapy [40]. The key to centrosome cluster destruction is getting therapeutic (toxic) nanoparticles to the clusters. The thesis advanced herein is that enhanced electropolarity of centrosome clusters will be an attraction for magnetically charged nanoparticles.

With nanoparticles being sufficiently small so that they can penetrate cell membranes, the nanoparticle size can arbitrarily be enlarged so that normal cell penetration is avoided, but cancer cells can be penetrated due to the electromagnetic attraction.

Although much remains to be done before this technology is efficacious, the steps forward are clear: More accurate empirical data is needed on the electromagnetic properties of microtubules, centrioles and centrosomes, and centrosome clusters. This data in turn will dictate the necessary additional testing and the development of the more effective nanoparticles.

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