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Active drug targeting

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Abstract of poster presented orally in the moderated poster session at the International Open NanoScience Congress, 26.2.2019, Salzburg (www.uni-salzburg.at/ONSC)

Over 100 years ago, Paul Ehrlich first proposed the side-chain theory to explain how living cells mount an immune response in reaction to an infection. His theory stated that upon the encounter of a threat, cells express side-chains to bind dangerous toxins. These side-chains, which he later named receptors, can break off the cell and circulate throughout the body (*i.e.* antibodies). Specific antibodies link to particular antigens in the same way that Emil Fischer proposed enzymes bind to their receptors, “as lock and key”. Ehrlich described these so-called “keys” or antibodies as “magic bullets”, which target toxins without harming the body. In recent years, research has focused on using antibodies not only for detection of infection, but also as aids for drug targeting. Thereby, antibodies are bound to the surface of carriers (*e.g.* nanoparticles) and facilitate a directed transport to a specific organ or site in the body. Aptamer-, peptide- or folic acid-doped carriers furthermore have been shown to specifically target cancer cells. By using hydrophilic structures as carriers (*e.g.* polyethylene glycol), negative side effects resulting from the accumulation of innate proteins can be prevented. Currently, there are drug carriers in the pre-clinical development phase for the treatment of bowel cancer. Thereby, nano polymer capsules coated with a specific antibody are used to target a glycoprotein expressed on bowel cancer cells. The polymers have a size of approximately 500 nm and are produced with a so-called “layer-by-layer” procedure. Once the carrier has reached its target site, the drug needs to be released in a controlled manner. This can be facilitated, for example, by applying a magnetic field in the case of iron oxide particles. Once these particles are taken up by the cells, magnetic radiation can be used to excite the particles, resulting in the rupture of the cell and subsequent cell death.

Keywords

Key-and-lock principle, Antibodies, Nanocarriers, Iron Oxide Particles, Therapeutics

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Aktives *Drug Targeting*

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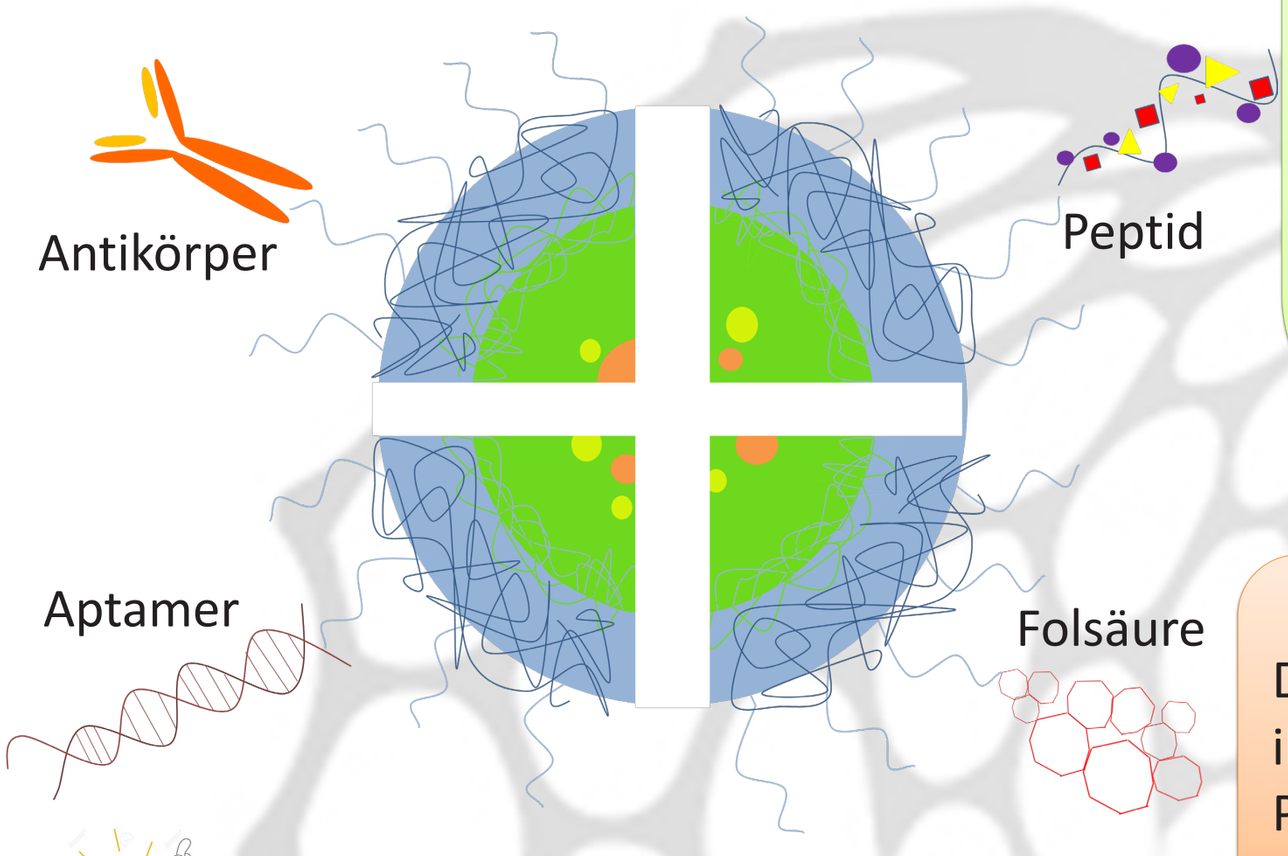
Hintergrund

Vor ca. 100 Jahren hatte Paul Ehrlich bereits die Vision von **„Zauberkugeln“** - Arzneistoffen, die spezifisch auf Krebszellen wirken und gesunde Zellen unbeschadet lassen ☞ Antikörper binden nach dem

„Schlüssel-Schloss“-Prinzip



☞ Aptamere sind kurze, einzelsträngige DNA- oder RNA-Sequenzen, die Strukturen annehmen und Liganden spezifisch binden können

Welche „Schlüssel“ gibt es?

Nanoträgerstoffe transportieren Therapeutika gezielt an ihr Zielorgan, z.B. mit Hilfe eines **Antikörpers**, der an die Oberfläche der Nanoträgerstoffe gebunden ist.

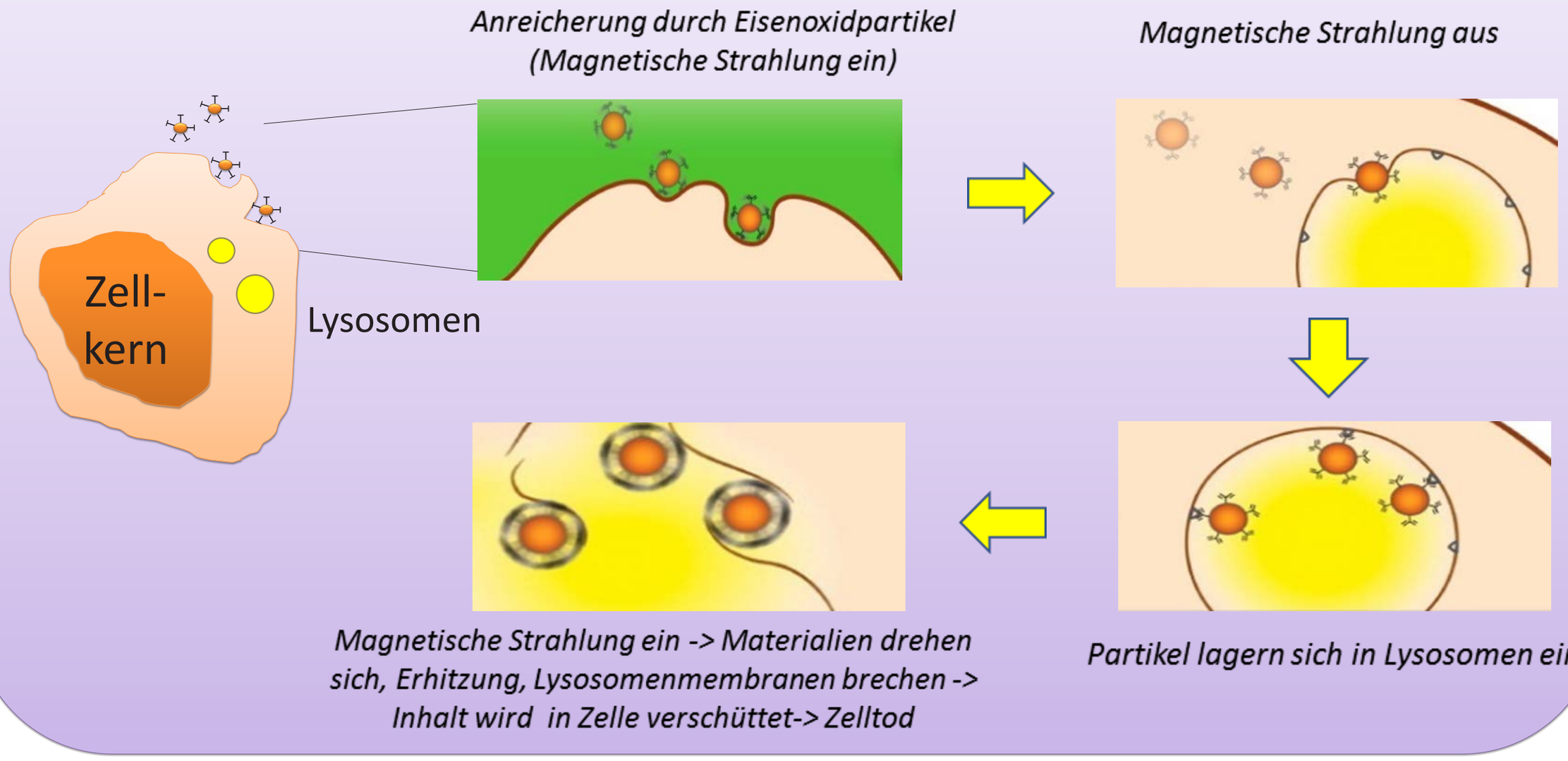
Alternativ binden **Aptamer-**, **Peptid-** oder **Folsäure**-dotierte Trägerstoffe spezifisch an Krebszellen.

Die Oberfläche ist mit **hydrophilen** Strukturen versehen, um Nebenwirkungen zu minimieren und die Anlagerung von körpereigenen Proteinen zu verhindern (Polyethylenglykol).

In präklinischer Entwicklung

Darmkrebszellen reichern Glykoprotein A33 auf ihrer Oberfläche an ☞ anti-A33-dotierte Nano-Polymerkapseln (~500 nm), mittels „Schicht-für-Schicht“-Verfahren hergestellt, binden spezifisch

Freisetzung des Therapeutikums aus Lysosomen mittels Magnetfeld



BMBWF
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