Preclinical developments in molecular imaging and potential clinical applications.

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Introduction

The ability to observe and statistically assess the operation of biological and cellular processes in vivo is referred to as molecular imaging. The rapidly developing field of molecular imaging promises advancements in specificity and quantitation for screening and early diagnosis, focused and personalised therapy, and earlier treatment follow-up. Anatomical imaging still plays a significant role in medical imaging for diagnosis, surgical guidance/followup, and treatment monitoring [1].

EGFR and HER2/neu, mammalian target of rapamycin, oestrogen receptor, and/or histone deacetylase are just a few examples of recent chemotherapeutic drug combinations used to treat breast cancer; however, the most successful approach depends on the molecular makeup of the tumour. Without the invasiveness of a surgical biopsy and the time required for pathological characterization, in vivo molecular imaging can be employed to determine and quantify the molecular marker profile of the tumour. For patients with advanced stage tumours and poor prognoses, the personalised medicine approach is crucial because in these cases, the danger of experiencing undesired side effects from treatment may outweigh the quality of life the patient will have left [2].

Recent preclinical improvements in molecular imaging contrast agents have shown the capacity to multiplex nano- and/or microparticles with various entities a molecule for targeting to a particular tissue/disease marker a direct attachment or system, for targeted delivery of a therapeutic drug at the site of interest. As an illustration, Blanco et al.4 describe the direct attachment of the chemotherapy drug, Doxirubicin, to a superparamagnetic iron oxide (SPIO) nanoparticle, which is then encapulated in liposomes coated with RGD-peptides. As a result, these particles specifically attach to tumour angiogenic vessels expressing high levels of V3-integrins [3].

Optical molecular imaging

Preclinical research employs a wide range of optical-based molecular imaging methods to characterise and comprehend biology as well as assess the molecular targets of contrast agents and/or therapies. Although optical imaging isn't frequently employed in clinical settings right now, there are a number of new technologies that support clinical translation. These "smart" probes use a dye-quencher system in which a brief linker peptide connects a fluorescent dye to a quenching molecule. The dye and quencher molecules separate when proteases cleave the peptide by a distance greater than 100 and the dye then transfers energy to the quencher causing the release of light. Since light is only released when the probe has reached its target and is activated, the "smart" probe strategy has great potential for clinical application. As a result, high signal-to-noise ratios can be obtained due to low background signal and minimal non-specific enzymatic cleavage, which is crucial for imaging weak optical imaging signals in the human body [4].

Acoustic molecular imaging

While preclinical research is concentrated on advancing this technology to a molecular-based approach, contrast-enhanced ultrasound is becoming more and more well-liked and supported for a number of clinical applications in both cardiology and radiology. Microvessels in tumours or inflamed tissues are examples of tissue vasculature where microbubbles can be molecularly targeted to disease-specific markers produced. Microbubbles with a streptavidin, avidin, or biotin moiety integrated into the lipid shell via a polyethylene glycol arm are the most common type used in preclinical molecular ultrasound imaging studies. These microbubbles are used to conjugate an antibody using a strept (avidin)-biotin chemistry. Nonetheless, because strept (avidin) is immunogenic, these microbubbles cannot be employed on people. Yet, the accessibility of antibodies and the simplicity of conjugating them to microbubbles serve as a foundation for proof-of-concept pre-clinical trials. Many studies have used microbubbles linked to an antibody or peptide, biotin-strept (avidin), to scan tumour angiogenic markers like VEGFR2, integrins, and endoglin. They include mucosal addressin cellular adhesion molecule, vascular cellular adhesion molecule, intracellular adhesion molecule, and P-selectin. Other researches have employed molecular-targeted microbubbles to scan molecular adhesion molecules overexpressed in microvessels of inflamed tissues.

The development of molecular-targeted microbubbles without the hazardous strept (avidin)-biotin chemistry, the implementation of quantitative software on clinical ultrasound machines, and a standardised method for quantifying attached microbubbles are three crucial steps in the clinical translation of molecular ultrasound imaging with microbubbles. Recently, a novel microbubble that targets the human equivalent of VEGFR2, known as the kinase insert domain receptor (KDR),

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was created by combining a heteropeptide that has been found to bind KDR with a high affinity with a hydrophilic spacer and lipid to form a heterolipopeptide that can be attached to the PEG arm of the microbubble shell. This contrast microbubble's preclinical testing revealed cross-reactivity with mouse VEGFR2 and the capacity to track anti-angiogenic therapy in mice with human colon tumors, 30 laying the framework for its eventual translation into clinical uses such tracking anti-angiogenic cancer therapy [5].

Conclusion

All areas of medical imaging, including early detection/screening, diagnosis, and therapy delivery/monitoring, and treatment follow-up, can benefit from the use of molecular imaging. Clinical molecular imaging is now in a limited state, with the majority of applications use PET and SPECT imaging, and only a tiny number of extremely specialised applications utilising MRI/MRS, optical, and ultrasound. New approaches are required to address current demands and trends, which include earlier disease detection through enhanced imaging and screening protocols, patient-specific treatment selection, delivery, and therapy-specific monitoring. It is envisaged that these new approaches to early diagnosis and close treatment monitoring would increase the likelihood of successfully treating diseases with high death rates, such as cancer and cardiovascular disease, and will also enable more targeted treatment for other illnesses.

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