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Nuclear Medicine; Cellular Homing and Traffic

Author

Dr. Didier Blocklet

Cellular and molecular therapy is one of the fastest growing fields of original clinical research. Pinpointing the traffic and homing of cellular compounds following administration is proving to be of immense importance, as these substances generally target specific organs where they have a set role to play. Research teams strive to ensure that the injected cells fulfil their therapeutic role, through in-vitro and animal studies. However, a number of problems arise when studying cellular traffic in humans, and these can begin at the site of administration, which should not be too invasive. What point is there in the cell being equipped to fulfil its role if it cannot reach the desired site of action?

For many years, radiopharmaceuticals used in nuclear medicine have enabled the in-vitro or in-vivo labelling of various types of blood cells, specifically, polynuclears and erythrocytes, in addition to the in-vivo study of cell traffic in patients suffering from various diseases. The route of administration (usually intravenous) permits easy access, whilst gamma camera imaging is straightforward to operate and is a technique in which many nuclear medicine units have considerable 'hands-on' experience. In practise, only cellular labelling requires a laboratory equipped with a laminar flow hood.

Alongside their routine examinations, clinical researchers have started to exploit these familiar clinical tools by the radiopharmaceutical labelling of other types of cell, which can then be studied in a similar way. Recently, for example, the long-awaited dream of setting off an immune reaction directed against neoplasias has taken shape through what is known as 'anti-tumour vaccination' using autologous dendritic cells (DC). By employing Indium-111 to label DC-carrying tumor antigens (loaded DC), researchers have shown that these cells, injected at the proximal part of limbs, migrate towards the regional lymph nodes (1). These lymph nodes definitely represent the expected target for the DCs since they constitute the point at which antigens are presented to the T4 lymphocytes, the essential first stage for triggering immune reaction and then anti-tumour immunity. In addition, a histological analysis of these lymph nodes, in combination with a microscopic study of the distribution of Indium-111 using autoradiography, established not only that these DCs reached the lymph nodes, but also that the DCs were present in the T-zones within the nodes. Once a tool of this type is available, it becomes easy to study this same cellular traffic in other types of DC or by varying the experimental conditions.

The development of radiopharmaceutical chemistry, specifically the introduction of peptide radiopharmaceuticals, ensures that we are no longer restricted to 'non-specific' radiotracers such as Indium-111, which are only able to fix to cellular cytoplasm. More specific tracers may be developed, able to label individual metabolic pathways, or identify one component within the membrane, which, in turn, will help refine research into traffic. A major advantage of radioactive tracers is their very high specific activity (i.e. the quantity of radioactivity per gram) which permits very small traces of radiopharmaceutical agents to be detected. This is very important in cellular labelling, as the tracer used must not modify cell viability or cell function. Patient irradiation can be evaluated with exclusive reference to the radiopharmaceutical agent and the form in which the radioactivity was administered. Imaging can then be repeated indefinitely, for as long as the signal can be detected, since the system for detecting gamma photons does not induce any additional radiation exposure. As a result dynamic acquisitions can be made, beginning at time zero, on different regions of the body, enabling the real-time, chronological study of bio-distribution (2).

These new developments involve the chemistry of both traditional gamma emitters and positron emitters. The latter permits PET imaging to be used, whose sensitivity and spatial resolution is greater. This equipment represents a reliable tool for quantification in both dynamic and non-dynamic acquisition mode (quantitative study of distribution). Combined PET/CT, now widely available, enhances the performance of CT - in particular its anatomical resolution - by means of image co-registration. These imaging studies can be complemented by histological evaluation of the tissue and sub-cellular distribution of tracer elements, through autoradiography on micro- and macroscopic sections. These can also be evaluated quantitatively.

The contribution made by nuclear medicine appears very promising in various fields of research, where a better understanding of cellular traffic is required. Throughout the world, a number of studies are already under way, including micro- and macroscopic imaging and bio-distribution, in both animals and humans.

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