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Central Role of Nuclear Medicine in Personalised Medicine

Molecular radionuclide imaging and therapies have a central role in the management of some oncological diseases, in particular they find a central application in neuroendocrine tumours (NETs). Peptide receptor imaging is a fundamental part of the tumour staging, preoperative imaging, therapy selection and restaging. Using the same drug, labelled with a different radionuclide, it's possible to offer a therapeutic option that is specific to the characteristics of the patient and his/her neoplasm. This is a model of personalised medicine is spreading more and more, due to the reduction of side effects and the promising results on the prognosis of patients.

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key points

- Precision medicine is a medical model that proposes the personalisation of healthcare, with medical decisions and practices tailored to the patient. In this context theragnostic is based on diagnostic molecular imaging, followed by an individually personalised treatment plans.
- Well-differentiated neuroendocrine tumours are characterised by the presence of a peculiar receptor that can be used as a "target" for diagnosis and selection of therapy.
- Peptide receptor radionuclide therapy has achieved such encouraging results in patients with neuroendocrine tumours that the scientific research suggests that the number of cancer patients with the characteristics to benefit from radionuclide therapies could significantly increase in the near future, including prostate cancer, breast, lung and pancreatic cancer.

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Theragnostic in Neuroendocrine Tumours

Theragnostic is the best example of the tailored medicine today, because it brings together the two pillars of this science namely Therapy and Diagnosis, combined into one weapon with a single target: to preserve patients' health.

Tailored medicine focused on more specific algorithms for different kinds of pathology contributes to developing several advances in surgery, medicine, and radiotherapy with excellent perspectives for the future, mainly in the oncological field.

In this scenario, the approach to cancer disease is changing thanks to an ever-increasing understanding of how malignant and healthy cells differ and how they interact with the surrounding micro-environment.

Drugs against specific "targets" are able to detect and to act directly on the diseased cells, reducing damage to healthy cells and consequently decrease side effects.

Based on this knowledge, cancer diagnostics and therapy are developing in an integrated way, going hand in hand rather than separately. In this era of precision medicine, which aims to find more accurate, safer, and personalised pathways, the concept of theragnostic has found its niche in the field of nuclear medicine, an imaging field that uses radioisotopes for molecular imaging and therapeutic purposes, with the possibility of labelling the same ligand with radionuclides with different characteristics, so as to allow staging, risk stratification, therapy selection and interventions, and response monitoring.

The first and the most promising example of a theragnostic application uses peptide receptor imaging and peptide receptor radionuclide therapy (PRRT) for neuroendocrine tumours (NET).

Neuroendocrine neoplasms (NEN) represent a heterogeneous group of tumours deriving from endocrine cells with the capacity to produce bioactive molecules. Even if NENs can occur in almost every tissue or district of the body, most of them originate from the digestive system, in particular from the gastroenteropancreatic (GEP) tract.

The classification of these neoplasms is based on proliferation index and cells' morphology, accordingly, the prognosis and behaviour are generally favourable in well-differentiated NETs (G1, G2 and G3) depending on grading, whereas low-differentiated tumours and neuroendocrine carcinomas (NEC) have an adverse outcome. Often NETs are non-secreting and late diagnosis is frequent, due their asymptomatic presentation, and therefore most of them present with advanced disease (Hallet J et al. 2015). NETs can differ in clinical symptoms and biology; however, they have specific markers of neuroendocrine cells and more than 80% of them over-express somatostatin receptors (SSTR) on cell surface (Kulaksiz H et al. 2002).

This discovery of the over-expression of SSTRs in NETs has led to the development of radiolabelled somatostatin analogues for diagnostic imaging at first. Thanks to technological advances, the current imaging methodologies have a high diagnostic performance and high accuracy. Today, the clinical scenarios in which peptide receptor imaging has definite value are the initial staging of well-differentiated NETs, identification of the primary tumour in patients who have neuroendocrine metastases of unknown origin and defining eligibility of patients for PRRT (Pavel M et al. 2020).

The introduction of PRRT is more recent than its imaging counterpart and requires that the diagnostic radionuclide is replaced with a therapeutic radionuclide, which has a different kind of radioactive emission, in the radiolabelled somatostatin analogues (Strosberg J et al. 2017). Once administered to a patient, the therapeutic radiopeptide binds to the neuroendocrine tumour cells that express SSTRs, then the constituted radiopeptide-receptor complex is internalised by the diseased cell, entrapping the radionuclide that acts locally and kills the tumour cell.

This innovative therapeutic option is most successful in patients with well-differentiated NETs that are low or intermediate grade and have over-expression of SSTRs as depicted on peptide receptor imaging.

The management of patients with NENs generally takes place in a multidisciplinary setting and it is in this context that the decision is made whether to treat an eligible patient with PRRT, considering several factors: therapy is usually prescribed in patients with inoperable tumours or with metastases at numerous sites and disease progression despite standard treatment. Unlike other treatment choices, PRRT has been shown to be effective in increasing overall survival, moreover, it has been demonstrated that it has positive effects also on progression-free survival and quality of life of patients, reducing the production of hormones with improvement of symptoms (Werner RA et al. 2015). Among other advantages, PRRT has few adverse side effects that are generally easily managed and has a favourable toxicity profile even in patients with disseminated disease.

The excellent results of the theragnostic approach in the management of neuroendocrine tumours, which for decades have had no valid therapeutic options to improve the prognosis, have paved the way for the search for new molecular targets for the treatment and diagnosis of other types of tumours.

Conclusion

Peptide receptor imaging and PRRT are a new frontier in personalised medicine because they allow for tailoring treatment plans to the unique features of the patient and the molecular characteristics of the tumour.

Many lessons have been learned from the progress in this field, and they may be the basis for developing new technologies. Probably theragnostic is more than an innovative approach because it will be able to change the course of many lives bringing hope even for diseases currently without an effective cure.

Conflict of Interest

None. ■

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