

Peptide targeting of lysophosphatidylinositol-sensing GPR55 for osteoclastogenesis tuning

Stefania Mariggiò, PhD
Institute of Biochemistry and Cell Biology, National Research Council, Naples, Italy

The G-protein-coupled receptor GPR55 has been implicated in multiple biological activities, which has fuelled interest in its functional targeting. Its controversial pharmacology and often species-dependent regulation have impacted upon the potential translation of preclinical data involving GPR55. With the aim to identify novel GPR55 regulators, we have investigated lysophosphatidylinositol (LPI)-induced GPR55-mediated signal transduction. The LPI/GPR55 axis was shown to have an active role in osteoclastogenesis of precursor RAW264.7 cells induced by 'receptor-activator of nuclear factor kappa-β ligand' (RANKL). Indeed, this differentiation into mature osteoclasts was associated with a 14-fold increase in Gpr55 mRNA levels. Moreover, GPR55 silencing and antagonism impaired RANKL-induced transcription of the osteoclastogenesis markers: 'nuclear factor of activated T-cells, cytoplasmic 1', matrix metalloproteinase-9, cathepsin-K, tartrate-resistant acid phosphatase, and the calcitonin receptor, as evaluated by real-time PCR. Phage display was previously used to identify peptides that bind to GPR55. Here, the GPR55-specific peptide-P1 strongly inhibited osteoclast maturation of RAW264.7 macrophages, confirming its activity as a blocker of GPR55-mediated functions. Although osteoclast syncytium formation was not affected by pharmacological regulation of GPR55, osteoclast activity was dependent on GPR55 signalling, as shown with resorption assays on bone slices, where LPI stimulated and GPR55 antagonists inhibited bone erosion. Our data indicate that GPR55 represents a target for development of novel therapeutic approaches for treatment of pathological conditions caused by osteoclast-exacerbated bone degradation, such as in osteoporosis or during establishment of bone metastases.

Biography

Stefania Mariggiò has completed her PhD with the Open University (London, UK) in 2001 and later on has been visiting Researcher at the University of Wisconsin (Madison, WI, USA) and at the Brigham and Women's Hospital (Harvard Medical School of Boston, MA, USA). She is Pricipal Investigator in the Laboratory of ‘Lysophospholipid Signalling for the Development of new Therapeutic Strategies’ of the Institute of Biochemistry and Cell Biology, National Research Council (Naples, Italy). She has published more than 39 papers in international journals and has been serving as Reviewer for several Journals and as an editorial board member of Frontiers.

Presenting author details

Full name: Stefania Mariggiò
Contact number: +39 0816132545/215
Orcid number: https://orcid.org/0000-0002-6397-3016
Session name/ number: Cancer Chemotherapy (Cancer Therapeutics, Novel and experimental approaches)/ Track 13-2
Category: Oral presentation