**Development of PET Molecular Probes for Lysophosphatidic Acid Receptor Type 1**

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Lysophosphatidic Acid Receptor 1 (LPA1) is one of the GPCR targets that is under-exploited for diagnostics and therapeutics with only a few ligands being developed. LPA1 is modulated by lysophosphatidic acid (LPA) which is a pleiotropic bioactive lipid presenting in nearly all cells, fluids, and tissues of the body [1]. LPA exerts a wide range of cellular responses, such as calcium mobilization, cell proliferation, migration, and chemotaxis via acting on LPA receptors [2]. The LPA receptors consist of six family members designated LPA1-LPA6. Among them, LPA1/2/3 from the EDG (endothelial differentiation gene) family shares a relatively high homology. It has been revealed that targeted deletion of the LPA1 on every organ system studied resulted in physiological effects that were linked to a range of diseases including cancer, pain, infertility, fibrosis, and hydrocephalus [3]. Moreover, LPA1 is highly expressed in breast carcinoma and prostate cancer, and the expression of LPA1 is significantly higher in human hepatocellular carcinoma than non-tumor liver [4]. The development of small molecules and positron emission tomography agents targeting LPA1 will provide powerful tools to study the receptor function and density related to those diseases. 11C-BMT-136088, the only one LPA1 radioligand developed to date showed high liver uptake on rhesus monkeys [5]. The aim of this study is to develop novel small molecule modulators and molecular imaging agents to study LPA1 related biological processes *in vivo*. We started with N-aryltriazole derived LPA1 ligands initially discovered by Roche for the treatment of idiopathic lung fibrosis [6] and designed a series of compounds with low binding free energy guided by computational molecular modelling. Multiple compounds bearing fluorine atom have been synthesized successfully. Candidate molecules with desirable binding affinity will be radiolabeled with 18F, and evaluated *in* *vivo* using mouse models of diseases with PET. The radiotracer will be useful for quantifying receptor density *in vivo* and studying LPA1-related cancers for developing LPA1-targeting drugs.

**Reference:**

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