

Synthesis, Characterization, and Biological Verification of Asialoglycoprotein Receptor-Targeted Lipopolysaccharides-Encapsulated PLGA Nanoparticles for Establishment of Liver Fibrosis Animal Model

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## ■ Supplementary Materials

**Table S1.** Top 100 significant signaling pathways found in both free LPS- and ALPNDs-treated groups based on NGS analysis.

| Rank | Molecular Pathways   | -log(p-value) | Ratio |
|------|--|---------------|-------|
| 1    | Neuroinflammation Signaling Pathway  | 21.9          | 0.202 |
| 2    | Pathogen Induced Cytokine Storm Signaling Pathway                              | 19.5          | 0.178 |
| 3    | Leukocyte Extravasation Signaling  | 16.6          | 0.223 |
| 4    | Phagosome Formation  | 14.9          | 0.124 |
| 5    | Macrophage Alternative Activation Signaling Pathway                            | 14.3          | 0.203 |
| 6    | TREM1 Signaling  | 13.9          | 0.325 |
| 7    | IL-12 Signaling and Production in Macrophages                                  | 13.9          | 0.186 |
| 8    | PD-1, PD-L1 cancer immunotherapy pathway                                       | 12.9          | 0.262 |
| 9    | Fcγ Receptor-mediated Phagocytosis in Macrophages and Monocytes                | 11.7          | 0.266 |
| 10   | MSP-ROn Signaling In Macrophages Pathway                                       | 10.8          | 0.227 |
| 11   | Role of Pattern Recognition Receptors in Recognition of Bacteria and Viruses   | 10.7          | 0.199 |
| 12   | Th1 Pathway  | 10.6          | 0.221 |
| 13   | Neutrophil Extracellular Trap Signaling Pathway                                | 10.4          | 0.131 |
| 14   | Atherosclerosis Signaling  | 10.4          | 0.211 |
| 15   | Role Of Osteoclasts In Rheumatoid Arthritis Signaling Pathway                  | 10.3          | 0.146 |
| 16   | Th1 and Th2 Activation Pathway   | 10.3          | 0.186 |
| 17   | S100 Family Signaling Pathway  | 10.2          | 0.105 |
| 18   | IL-10 Signaling  | 9.51          | 0.188 |
| 19   | Colorectal Cancer Metastasis Signaling   | 9.44          | 0.148 |
| 20   | Th2 Pathway  | 9.36          | 0.197 |
| 21   | Multiple Sclerosis Signaling Pathway   | 9.12          | 0.158 |
| 22   | Production of Nitric Oxide and Reactive Oxygen Species in Macrophages          | 9.07          | 0.168 |
| 23   | IL-8 Signaling   | 8.6           | 0.157 |
| 24   | Endothelin-1 Signaling   | 8.3           | 0.16  |
| 25   | Role of Macrophages, Fibroblasts and Endothelial Cells in Rheumatoid Arthritis | 7.83          | 0.127 |
| 26   | Hepatic Fibrosis Signaling Pathway   | 7.76          | 0.116 |

|    |   |      |        |
|----|---|------|--------|
| 27 | Eicosanoid Signaling  | 7.54 | 0.243  |
| 28 | Granulocyte Adhesion and Diapedesis                                       | 7.4  | 0.153  |
| 29 | Tumor Microenvironment Pathway  | 7.36 | 0.156  |
| 30 | Crosstalk between Dendritic Cells and Natural Killer Cells                | 7.21 | 0.209  |
| 31 | Axonal Guidance Signaling   | 7.17 | 0.106  |
| 32 | Pyroptosis Signaling Pathway  | 7.05 | 0.204  |
| 33 | HIF1 $\alpha$ Signaling   | 7.02 | 0.144  |
| 34 | LXR/RXR Activation  | 6.96 | 0.179  |
| 35 | Natural Killer Cell Signaling   | 6.95 | 0.146  |
| 36 | G-Protein Coupled Receptor Signaling                                      | 6.93 | 0.0953 |
| 37 | Sperm Motility  | 6.93 | 0.132  |
| 38 | Macrophage Classical Activation Signaling Pathway                         | 6.84 | 0.148  |
| 39 | Role of JAK1 and JAK3 in $\gamma$ c Cytokine Signaling                    | 6.84 | 0.232  |
| 40 | Phospholipases  | 6.84 | 0.232  |
| 41 | Toll-like Receptor Signaling  | 6.8  | 0.218  |
| 42 | Glucocorticoid Receptor Signaling   | 6.72 | 0.0997 |
| 43 | Role of Osteoblasts, Osteoclasts and Chondrocytes in Rheumatoid Arthritis | 6.64 | 0.136  |
| 44 | Signaling by Rho Family GTPases   | 6.53 | 0.127  |
| 45 | Agranulocyte Adhesion and Diapedesis                                      | 6.4  | 0.138  |
| 46 | PI3K/AKT Signaling  | 6.32 | 0.14   |
| 47 | MSP-RON Signaling Pathway   | 6.29 | 0.241  |
| 48 | Antioxidant Action of Vitamin C   | 6.25 | 0.175  |
| 49 | Molecular Mechanisms of Cancer  | 6.13 | 0.104  |
| 50 | Fc Epsilon RI Signaling   | 6    | 0.169  |
| 51 | Cardiac Hypertrophy Signaling (Enhanced)                                  | 5.94 | 0.0978 |
| 52 | Antigen Presentation Pathway  | 5.79 | 0.282  |
| 53 | ID1 Signaling Pathway   | 5.77 | 0.134  |
| 54 | IL-9 Signaling  | 5.37 | 0.286  |
| 55 | Role Of Chondrocytes In Rheumatoid Arthritis Signaling Pathway            | 5.33 | 0.149  |
| 56 | CDX Gastrointestinal Cancer Signaling Pathway                             | 5.23 | 0.129  |
| 57 | ERK/MAPK Signaling  | 5.21 | 0.126  |
| 58 | Hepatic Cholestasis   | 5.19 | 0.131  |
| 59 | CREB Signaling in Neurons   | 5.14 | 0.0906 |
| 60 | Ceramide Signaling  | 5.14 | 0.176  |
| 61 | Thrombopoietin Signaling  | 5.07 | 0.206  |
| 62 | Hepatic Fibrosis / Hepatic Stellate Cell Activation                       | 5.06 | 0.129  |
| 63 | VEGF Family Ligand-Receptor Interactions                                  | 4.94 | 0.179  |
| 64 | iNOS Signaling  | 4.93 | 0.234  |
| 65 | GP6 Signaling Pathway   | 4.91 | 0.15   |
| 66 | Osteoarthritis Pathway  | 4.9  | 0.119  |
| 67 | Oxytocin In Brain Signaling Pathway                                       | 4.87 | 0.126  |
| 68 | Chronic Myeloid Leukemia Signaling  | 4.81 | 0.112  |
| 69 | Breast Cancer Regulation by Stathmin1                                     | 4.79 | 0.0892 |
| 70 | NOD1/2 Signaling Pathway  | 4.78 | 0.127  |
| 71 | Erythropoietin Signaling Pathway  | 4.77 | 0.13   |
| 72 | Sphingosine-1-phosphate Signaling   | 4.7  | 0.15   |
| 73 | p38 MAPK Signaling  | 4.7  | 0.15   |

|     |   |      |       |
|-----|---|------|-------|
| 74  | IL-7 Signaling Pathway  | 4.68 | 0.179 |
| 75  | Regulation Of The Epithelial Mesenchymal Transition By Growth Factors Pathway | 4.67 | 0.125 |
| 76  | Primary Immunodeficiency Signaling  | 4.66 | 0.203 |
| 77  | Actin Cytoskeleton Signaling  | 4.63 | 0.115 |
| 78  | IL-3 Signaling  | 4.61 | 0.177 |
| 79  | RHOGDI Signaling  | 4.57 | 0.118 |
| 80  | Gαq Signaling   | 4.56 | 0.129 |
| 81  | IL-15 Production  | 4.56 | 0.146 |
| 82  | Inflammasome pathway  | 4.55 | 0.35  |
| 83  | GM-CSF Signaling  | 4.55 | 0.186 |
| 84  | RAC Signaling   | 4.44 | 0.139 |
| 85  | MIF Regulation of Innate Immunity   | 4.41 | 0.227 |
| 86  | IL-17 Signaling   | 4.39 | 0.123 |
| 87  | Role of Tissue Factor in Cancer   | 4.35 | 0.147 |
| 88  | Complement System   | 4.28 | 0.243 |
| 89  | Virus Entry via Endocytic Pathways  | 4.25 | 0.144 |
| 90  | Paxillin Signaling  | 4.23 | 0.15  |
| 91  | Caveolar-mediated Endocytosis Signaling                                       | 4.22 | 0.173 |
| 92  | HMGB1 Signaling   | 4.2  | 0.126 |
| 93  | fMLP Signaling in Neutrophils   | 4.19 | 0.137 |
| 94  | CXCR4 Signaling   | 4.16 | 0.125 |
| 95  | Leptin Signaling in Obesity   | 4.16 | 0.171 |
| 96  | GDNF Family Ligand-Receptor Interactions                                      | 4.16 | 0.171 |
| 97  | Macropinocytosis Signaling  | 4.16 | 0.171 |
| 98  | P2Y Purigenic Receptor Signaling Pathway                                      | 4.1  | 0.135 |
| 99  | VEGF Signaling  | 4.07 | 0.152 |
| 100 | STAT3 Pathway   | 4.01 | 0.133 |