심혈관 환자맞춤형 차세대 정밀의료기술 선도연구센터(RLRC)
2단계 2차년도 정기세미나

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❍ **연사** : 연세대학교 의과대학 의생명과학부 이신정 교수

❍ **주제** : Preclinical study of human induced pluripotent stem cell-derived endothelial cells for peripheral artery disease

❍ **Abstract** : Peripheral artery disease (PAD), affecting over 230 million people globally, can progress to chronic limb-threatening ischemia (CLTI), a condition often resulting in limb amputation. Human induced pluripotent stem cell-derived endothelial cells (hiPSC-ECs) have emerged as a promising regenerative therapy for PAD; however, their clinical use remains limited due to the absence of regulatory criteria and preclinical validation. To address this, we conducted a comprehensive study evaluating the feasibility, efficacy, and safety of clinical-grade hiPSC-ECs generated from PAD patients in the context of developing future autologous therapies.We reprogrammed peripheral blood mononuclear cells from three PAD patients into hiPSC lines using episomal plasmids. These lines exhibited stable karyotypes, expressed pluripotency markers, and formed teratomas. Directed differentiation yielded hiPSC-ECs that displayed cobblestone morphology, expressed endothelial markers (CDH5: 98.4 ± 0.2%, VWF: 94.4 ± 1.3%), and maintained genomic stability confirmed by CGH array. Functional assays revealed robust nitric oxide production and tube formation. In a murine hindlimb ischemia model, PAD-hiPSC-ECs significantly improved perfusion (~3.3-fold), reduced limb loss (~8.8 ±0.6%), and enhanced vascular density (~2.7-fold) versus controls. Long-term toxicity, biodistribution, and tumorigenicity assessments in nude mice showed no adverse findings over 12 months. Based on these results, our cell therapy received regulatory approval for clinical trials in Korea targeting moderate-to-severe PAD and patient recruitment has begun. This first-in-field preclinical validation of autologous hiPSC-EC therapy demonstrates its therapeutic potential and safety, and provides critical translational and regulatory groundwork for clinical applications.