CDB SEMINAR

Akitsu Hotta

CiRA, Kyoto University

Tuesday, November 27, 2012
16:00~17:00 A7F Seminar Room

Transposon Technologies Towards iPS Cell Gene Therapy

Summary

Patient-derived iPS cells hold a great potential for future *ex vivo* gene therapy. Viral vectors are widely used to deliver foreign genes because of their good transduction efficiencies. At the same time, viral vectors have been suffered from several issues, such as cargo-size limit, host immunological reactions and transcriptional silencing in pluripotent stem cells. In this regard, we utilize cabbage looper derived *piggyBac* DNA transposon vectors for expressing therapeutic genes in human iPS cells. Unexpectedly, we also observed similar transgene silencing of the *piggyBac* vectors in ES/iPS cells.

To dissect the molecular basis of the silencing, we have developed a novel genome-wide screening method using transposon-based shRNA library, in conjugation with deep sequencing technology. From our screenings, we have identified several candidate factors, including general transcriptional repressors that can reactivate *piggyBac* transgene after the shRNA treatment.

Furthermore, to overcome the silencing issue, we have incorporated the human D4Z4 insulator element, which is located at the subtelomeric region, into our *piggyBac* vectors. With D4Z4 insulator, we succeeded to maintain transgene expression in ES/iPS cells for over 160 days. Our vectors may have promising utilities for gene transfer applications including iPS cell gene therapy.

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