## Stem Cell & Regenerative Medicine 2018- Novel anti-cancer binary system activated by bacteriophage HK022 integrase

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ene therapy is a promising tool for cancer ther-Japeutics. However, a major obstacle that persists is the lack of specificity of the expressed toxic gene against cancer cells. Binary systems based on site-specific recombination are one of the most effective potential approaches for cancer gene therapy. In these systems, a cancer specific promoter expresses a site-specific recombinase/integrase that in turn controls the expression of a toxin gene. We have developed a new HK022 bacteriophage integrase (Int) based binary system that activates a diphtheria toxin (DTA) gene expression specifically in cancer cells (Fig 1. A). The efficiency, and specificity of the system were assessed in-vitro and in-vivo in a lung cancer mouse model. The system presents a significant efficiency and specificity in series of criteria. Strikingly, employment of the developed system to treat mice with lung cancer demonstrates significantly increased longevity (Fig.1 B). The molecular factors that contribute to the system specificity will be described.

**Conclusion:** Recombinase-activating gene (RAG) deficient SCID patients lack B and T lymphocytes due to the inability to rearrange immunoglobulin and T-cell receptor genes. The two RAG genes are acting as a required dimer to initiate gene recombination. Gene therapy is a valid treatment alternative for RAG-SCID patients, who lack a suitable bone marrow donor, but developing such therapy for RAG1/2 has proven challenging. Hence, we tested clinically relevant lentiviral SIN vectors with different internal promoters (UCOE, PGK, MND, and UCOE-MND) driving codon optimized versions of the RAG1 or RAG2 genes to ensure optimal expression. We used Rag1-/- or Rag2-/-mice as a preclinical model for RAG-SCID to assess the efficacy of the various vectors at low vector copy number. In

parallel, the-conditioning regimen in these mice was optimized using busulfan instead of commonly used total body irradiation. We observed that B and T cell reconstitution directly correlated with RAG1 and RAG2 expression. Mice receiving low Rag1/2 expression showed poor immune reconstitution; however high Rag1/2 expression resulted in a lymphocyte reconstitution comparable to mice receiving wild type stem cells. Efficiency and safety of our clinical RAG1 lentivirus batch was assessed in Rag1-/- mice model showing that functional restoration of RAG1-deficiency can be achieved with clinically acceptable vectors. Additionally, RAG1-SCID patient CD34+ cells transduced with our clinical RAG1 vector and transplanted into NSG mice led to fully restored human B and T cell development. Together with favorable safety data, these results substantiate a clinical trial for RAG1 SCID which is planned for late 2018.

The global Stem Cell market is expected to grow at an incredible CAGR of 25.5% from 2015 to 2022 and reach a market value of US\$297 billion by 2022. The emergence of Induced Pluripotent Stem (iPS) cells as an alternative to ESCs (embryonic stem cells), growth of developing markets, and evolution of new stem cell therapies represent promising growth opportunities for leading players in this sector. Due to the increased funding from Government and Private sector and rising global awareness about stem cell therapies and research are the main factors which are driving this market. A surge in therapeutic research activities funded by governments across the world has immensely propelled the global stem cells market. However, the high cost of stem cell treatment and stringent government regulations against the harvesting of stem cells are expected to restrain the growth of the global stem cells market.Whereas the Europe Stem cell market is estimated to grow at a CAGR of 9.45% by the end of the forecast period of 2018-2026. The market is chiefly progressing due to increasing R&D investments in adult stem cell research in the region, ease of administration and the growing incidences of chronic disease due to the changing lifestyles of the population.The countries analyzed in the Europe Stem cell market are UK, France, Germany, Spain, Italy and rest of Europe. Most of these countries have a stable economic environment, enabling their population to spend more on their health. In this report, the Europe stem cell market has been segmented based on technology, product and applications. At present, the regenerative medicine application accounts for a high revenue share. Because of their use in regenerative therapies, stem cells are increasingly finding applications in the fields of neurological and hematological disorders, and in areas such as organ transplants, Crohn's disease, systemic lupus, and infertility. The worldwide Stem cell & regenerative medicines market is functional with several parameters like product type, application, sources, geography and users. In focused to the product type stem cells market is divided into human embryonic stem cells, adult stem cells, IPsec's, etc. Whereas, regenerative medicines applied the potential of these stem cells to regenerate, repair & replace tissues or the organ which are affected due to injury, natural aging process, and some diseases.