Innovative Biotherapies

Trend Chart On Innovative Biotherapies

Date : December 2017, 10th

Content

Gene Therapy

Recombinant adeno-associated virus (rAAV) vectors are increasingly popular tools for gene therapy applications. Their non-pathogenic status, low inflammatory potential, availability of viral serotypes with different tissue tropisms, and prospective long-lasting gene expression are important attributes that make rAAVs safe and efficient therapeutic options. Over the last three decades, several groups have engineered recombinant AAV-producing platforms, yielding high titers of transducing vector particles. Current specific productivity yields from different platforms range from 10^3 to 10^5 vector genomes (vg) per cell, and there is an ongoing effort to improve vector yields in order to satisfy high product demands required for clinical trials and future commercialization. In a recent review, the rational design of rAAV-producing expression systems is discussed, with special attention to molecular strategies that contribute to high-yielding, biomanufacturing-amenable rAAV production processes.
The review appeared in December 04th online issue of Applied Microbiol Biotechnol.

Related Informations / Publications

Reference	Title	Authors	Location	Results / Comment	Link to Abstract
Methods Mol Biol. 2018;1715:19-31	Small and Micro-Scale Recombinant Adeno-Associated Virus Production and Purification for Ocular Gene Therapy Applications	Reid CA, Lipinski DM	University of Oxford, Oxford, UK	A method to produce high titer (10^{12}-10^{13} vector genomes (vg)/mL) rAAV vector on small (~100 µL) or micro (~15 µL) scale	Abstract
Hum Gene Ther Methods. 2017 Oct;28(5):235-246	Protocol for Efficient Generation and Characterization of Adeno-Associated Viral Vectors	Jungmann A, Leuchs B, Rommelaere J, Katus HA, Müller OJ	University of Kiel , Kiel, Germany	A step-by-step procedure that results in well-characterized vectors suitable for both in vitro approaches and preclinical studies	Abstract
Mol Ther. 2017 Dec 6;25(12):2661-2675	Direct Head-to-Head Evaluation of Recombinant Adeno-associated Viral Vectors Manufactured in	Kondratov O & al (11 authors)	University of Florida College of Medicine, Gainesville, FL 32610, USA	the described system yields rAAV vectors of superior infectivity and higher genetic identity providing a	Abstract

	Human versus Insect Cells			scalable platform for good manufacturing practice (GMP)-grade vector production.	

Clinical Trial

CRISPR Therapeutics announced on December 07th the submission of a Clinical Trial Application (CTA) for CTX001 in β-thalassemia. CTX001 is an investigational CRISPR gene-edited autologous hematopoietic stem cell therapy for patients suffering from beta-thalassemia and sickle cell disease. The phase I/II trial of CTX001 is designed to assess its safety and efficacy in adult transfusion dependent β-thalassemia patients and is expected to begin in Europe in 2018. CRISPR also plans to file an Investigational New Drug Application for CTX001 to treat sickle cell disease with the United States Food and Drug Administration in 2018. CTX001 is the first CRISPR/Cas9-based treatment to advance from a research program jointly conducted by CRISPR Therapeutics and Vertex Pharmaceuticals under the companies' collaboration aimed at the discovery and development of new gene editing treatments that use the CRISPR/Cas9 technology. Under the agreement, Vertex has exclusive rights to license up to six new CRISPR/Cas9-based treatments that emerge from the collaboration. For further info.

Related Informations / Publications

Date	Title	Collaboration / Company	Results / Comment	Link to Abstract / PR
NOV 2017	CRISPR Therapeutics and Casebia Collaborate with CureVac on mRNA for Gene-Editing Programs	Casebia, Curevac	CureVac's mRNA technology accessed to express Cas9 for in vivo liver-targeted therapies	Press release
OCT 2015	Vertex and CRISPR Therapeutics Establish Collaboration to Use CRISPR-Cas9 Gene Editing Technology	Vertex	Vertex will have exclusive rights to license up to six new CRISPR-Cas9-based treatments that emerge from the collaboration	BusinessWire

The prevention of bleeding with adequately sustained levels of clotting factor, after a single therapeutic intervention and without the need for further medical intervention, represents an important goal in the treatment of hemophilia B. Researchers infused a single-stranded adeno-associated viral (AAV) vector consisting of a bioengineered capsid, liver-specific promoter and factor IX Padua (factor IX–R338L) transgene at a dose of 5×10^{11} vector genomes per kilogram of body weight in 10 men with hemophilia B who had factor IX coagulant activity of 2% or less of the normal value. Laboratory values, bleeding frequency, and consumption of factor IX concentrate were prospectively evaluated after vector infusion and were compared with baseline values. No serious adverse events occurred during or after vector infusion. Vector-derived factor IX coagulant activity was sustained in all the participants, This work was supported by Spark Therapeutics
Spark Therapeutics and Pfizer
The results appeared in December 07th online issue of New Engl J Med. For further info.

Related Informations / Publications

Date	Title	Collaboration / Company	Results / Comment	Link to Abstract / PR
NOV 2017	Spark Therapeutics and Pfizer Amend License Agreement for Investigational SPK-9001 in Hemophilia B	Pfizer	Spark Therapeutics to receive up to an additional $25 million per terms of amendment	Press Release
NOV 2017	Novel approaches to hemophilia therapy: successes and challenges	The Children's Hospital of Philadelphia (US)	New therapies for hemophilia A and hemophilia B will likely continue to change clinical practice	Abstract

Adverum Biotechnologies, of Menlo Park, Calif., said on December 05th that it has started the phase I/II ADVANCE trial testing ADVM-043 in up to 20 patients with alpha-1 antitrypsin deficiency (A1AT Deficiency). The study will test four doses of ADVM-043, a gene therapy that expresses the A1AT protein. Preliminary data from the trial are expected in the second half of 2018. For further info.

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Reference	Title	Authors	Location	Results / Comment	Link to Abstract
Mol Ther. 2017 Nov 1;25(11):2477-2489	Survival Advantage of Both Human Hepatocyte Xenografts and Genome-Edited Hepatocytes for Treatment of α-1 Antitrypsin Deficiency	Borel F, Tang Q, Gernoux G, Greer C, Wang Z, Barzel A, Kay MA, Shultz LD, Greiner DL, Flotte TR, Brehm MA, Mueller C	University of Massachusetts Medical School, Worcester, MA 01605, USA	This gene-editing approach leads to a selective advantage of edited hepatocytes, by silencing the mutant protein and augmenting normal AAT production, and improvement of the liver pathology.	Abstract
Mol Ther. 2017 Jun 7;25(6):1387-1394	5 Year Expression and Neutrophil Defect Repair after Gene Therapy in Alpha-1 Antitrypsin Deficiency	Mueller C, Gernoux G, Gruntman AM, Borel F, Reeves EP, Calcedo R, Rouhani FN, Yachnis A, Humphries M, Campbell-Thompson M, Messina L, Chulay JD, Trapnell B, Wilson JM, McElvaney NG, Flotte TR	University of Massachusetts Medical School, Worcester, MA 01655, USA	These findings suggest that muscle-based alpha-1 antitrypsin gene replacement is tolerogenic and that stable levels of M-AAT may exert beneficial neutrophil effects at lower concentrations than previously anticipated	Abstract
Curr Med Chem. 2017;24(1):65-90	Alpha-1 Antitrypsin Deficiency: Current Perspective from Genetics to Diagnosis and Therapeutic Approaches	Santangelo S, Scarlata S, Poeta ML, Bialas AJ, Paone G, Incalzi RA	Campus Bio Medico University and Teaching Hospital, Via Alvaro del Portillo 200, 00128 - Rome, Italy	Review	Abstract

Industrial Landscape / Agreements

The Cell and Gene Therapy Catapult, of London, in collaboration with Oxford Mestar, a U.K.-based bioengineering company specializing in process automation for the regenerative medicine and cell therapy sector, and AK (Suzhou) Biomedical, a Chinese biotech firm specializing in products and services for clinical applications that aim to support the development of a manufacturing system intended to reduce the cost of production of CAR T therapy, said on December 05th that they have been awarded a grant of £506,000 (US$680,509) from the Innovate UK-Jiangsu Industrial Challenge Program, a project set up by Innovate UK and Jiangsu Science and Technology Department to stimulate economic growth, and foster ties between China and the U.K. For further info.

Related Informations / Publications

Date	Title	Partners	Results / Comment	Link to Abstract / PR
OCT 2017	Cell and Gene Therapy Catapult Annual Review Reveals Burgeoning UK Cell and Gene Medicines Sector	NI	NI	Press Release
OCT 2017	UK's Cell and Gene Therapy Catapult Partners with Japan	Japan's Forum for Innovative Regenerative Medicine	Through this collaboration, FIRM and the CGT Catapult will share information regarding regenerative medicine technologies	BioPharm Int

Fortress Biotech, of New York, said on December 05th that it has formed Tamid Bio Inc., a subsidiary dedicated to the development of adeno-associated virus (AAV) gene therapies in orphan diseases with unmet medical needs. As part of its formation, Tamid has entered three exclusive licensing agreements with the University of North Carolina at Chapel Hill for three preclinical AAV gene therapies. Tamid's lead program, Tamid-001, targets the ocular manifestations of mucopolysaccharidosis type I, a rare and progressively debilitating disorder, caused by mutations in the IDUA gene, leading to the accumulation of glycosaminoglycans (GAGs) in multiple organs. For further info.

Related Informations / Publications

Date	Title	Partners	Results / Comment	Link to Abstract / PR
DEC 2017	Mustang Bio (a Fortess company) Announces License Agreement CRISPR/Cas9-Enhanced CAR T Therapies	Beth Israel Deaconess (IL), Harvard University US)	CAR T cell therapies for the development of treatments for hematologic malignancies and solid tumors	Press Release

Gilead Sciences and its cell therapy subsidiary Kite Pharma announced on December 07th that they have entered into a definitive agreement under which they have agreed to acquire Cell Design Labs, gaining new technology platforms that will enhance research and development efforts in cellular therapy. Under the terms of the agreement, Gilead will acquire all of the outstanding shares of Cell Design Labs, which includes the approximately 12.2 percent of shares of Cell Design Labs that are currently held by Kite, for up to approximately $567 million. For further info.

Related Informations / Publications

Date	Title	Partners	Results / Comment	Link to Abstract / PR
OCT 2017	Kite's Yescarta™ (Axicabtagene Ciloleucel) Becomes First CAR T Therapy Approved by the FDA		Relapsed or Refractory Large B-Cell Lymphoma After Two or More Lines of Systemic Therapy	Press Release
AUG 2017	Gilead Sciences to Acquire Kite Pharma for $11.9 Billion	Gilead Sciences, Kite Pharma	Acquisition	Press Release

Horizon Discovery Group, of Cambridge, U.K., and ERS Genomics, of Dublin, said on December 05tht that they extended their 2014 nonexclusive, worldwide license agreement to significantly expand Horizon's license coverage for the use of the CRISPR gene-editing technology. The move will enable Horizon to use CRISPR in multiple new areas across its products and services, providing access to additional revenue streams in new and existing markets, and further reinforcing Horizon's position in gene editing and cell biology, the companies said. Terms were not disclosed. For further info.

Related Informations / Publications

Date	Title	Partners	Results / Comment	Link to Abstract / PR
NOV 2017	ERS Genomics and Cellecta, Inc. Sign License Agreement on CRISPR/Cas9 Genome Editing Patents for Tools and Services	Cellecta	A non-exclusive license agreement to provide Cellecta with worldwide access to ERS Genomics' CRISPR/Cas9 genome editing intellectual property for use in informing research tools and services	prnewswire
JAN 2017	Horizon broadens industry-leading gene editing capabilities through extension of key CRISPR license	ERS Genomics	Access to CRISPR for the generation of GMP biomanufacturing cell lines through extension of existing ERS Genomics license	Press Release

	and grant-funded research			

Obsidian Therapeutics, a biotechnology company dedicated to the development of next-generation cell and gene therapies with pharmacologic operating systems, announced on December 06th the completion of a $49.5 million Series A financing to further build its technology platform and advance its lead programs toward clinical development. Obsidian was founded in 2015 by Atlas Venture, who exclusively funded the company's operations through mid-2017. The Series A financing was led by GV, with participation from Atlas Venture, as well as Takeda Ventures Inc., Vertex Ventures HC, Amgen Ventures, Alexandria Venture Investments, and ShangPharma Investment Group. The company has also named serial entrepreneur and biotechnology executive Michael Gilman, Ph.D., as Chief Executive Officer. Obsidian's initial areas of drug development include regulated cytokine cassettes for inclusion in CAR-T products to enhance anti-tumor activity and cellular persistence, as well as regulated CAR for enhancement of safety and anti-tumor efficacy. In these areas of focus, using DD technology enables control of key functions to improve safety and efficacy in ways that are not possible with existing CAR-T treatments. For further info.

Related Informations / Publications

Date	Title	Partners	Results / Comment	Link to Abstract / PR
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