GIOSTAR - CHICAGO
Institute of Stem Cell Therapy & Research

Summary

Dr. Anand Srivastava is the Co-Founder and Chief Scientific Officer of GIOSTAR. He has been involved in numerous studies, publications, and other activities to advance the field of regenerative medicine, and aid in the development of therapeutic approaches to the world's most devastating diseases.

The following document summarizes Dr Anand's major scientific achievements and publications.

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Dr. Anand's Full Biography is available at the [GIOSTAR Chicago Website].

A. Dr. Srivastava's Major Scientific Achievements

a. Dr. Srivastava developed the animal material free and serum free Human Embryonic Stem Cell (hESC) culture condition to use the hESC's to treat human diseases.

b. Dr. Srivastava **for the first time** showed that if the ES cell is injected into developing fetuses *in utero*, it participates in the development of all body of a living organism.

c. **For the first time** Dr. Srivastava showed that ES cell is better accepted by the transplanted animals in comparison to adult stem cells.

d. **For the first time** Dr. Srivastava showed the way to generate a high number of pre-erythrocytes using the glucocorticoid hormone; this method may be used to treat several blood diseases.

e. Using ES cells, Dr. Srivastava **for the first time** generated a high number of CD34+ expressing a kind of hematopoietic stem cell, which can be used to treat several autoimmune diseases, immune reconstitution and blood diseases.

f. **For the first time** Dr. Srivastava showed the molecular mechanism behind the regulation of ES cell differentiation into hematopoietic cells.

g. **For the first time** Dr. Srivastava showed that ES cells automatically recognize the damage portion of the brain and can be used to repair the damage brain.

h. **For the first time** Dr. Srivastava showed that ES cell can be used to treat Crohn's disease.

i. For the first time, Dr. Srivastava demonstrated that mammalian fetuses can be programmed inside the mother's uterus to face the challenges of future possible infection. This finding is very important in developing advanced therapy for any fatal disease, such as cancer and AIDS**.** Utilizing these techniques, fetuses can be given information about all possible infections and the capability to counter those infections and disease.

j. Dr. Srivastava demonstrated **for the first time** that it is easy to correct genetic diseases in developing fetus *in utero*, in comparison to adult animals.

k. Dr. Srivastava has shown **for the first time** that the lung cancer cells can be treated with the help of plant product curcumin, and can be used as an effective cancer therapeutic agent. He also demonstrated how curcumin regulated the genes related to programmed death of the cancerous cell. This would aid in the development of non-toxic, less expensive, easily available drugs for cancer.

l. The biggest problem in the treatment of cancer and other diseases is the non-specific distribution of medicine and toxic chemotherapeutic agents to healthy tissues. Dr. Srivastava **for the first time** developed a technique that can help in targeting the diseased tissues using the tissue receptor binding peptide ligands. These techniques can be used for targeted delivery of drugs and genes (in case of genetic disease) to the specific fetal tissues inside the mother uterus without harming the normal tissues of mother and fetus.

m. **For the first time**, Dr. Srivastava demonstrated the insertion of foreign pancreas enzyme specific gene promoter into the developing animal embryo, and successfully showed the incorporation and regulation of pancreatic enzyme in the control of inserted gene. This is a very important finding, and proves that the defective genes can be replaced easily and effectively by normal functional genes during the development of animals. This finding will aid in the change of defective genes of insulin hormone, which is present in the pancreas of diabetic patients and many other genetic diseases.

n. **For the first time**, Dr. Srivastava reported the gene sequence of all important pancreatic enzymes (three isoform of trypsinogen, two isoforms of chymotrypsinogen, four types of elastases, three forms of carboxypeptidases and lipase) and its evolutionary relationship with the human body. Also, he reported for the first first time the regulation of digestion by these enzymes in the alimentary canal, during the digestion of proteins in the developing animals.

o. **For the first time**, Dr. Srivastava cloned and sequenced two types of human homologue of Vitamin D receptor gene from Japanese flounder - the most important receptor, which helps in bone development. Before his report, characters of this gene were not known in Japanese flounder. This finding helped in the understanding of the genetic evolution of mammals.

p. **For the first time**, Dr. Srivastava cloned and sequenced the homologue of human placental protein, PP11, and mouse T cell specific, Tcl-30, in the pancreas of the Japanese flounder. This study suggests that these genes evolved from the fish pancreas, and in fish they help to synthesize digestive enzymes; during the evolution, however, their function got changed and led them to work differently in the mammalian placenta. This was a very important finding related to this rare gene.

q. **For the first time**, Dr. Srivastava showed that the Hox and sonic hedgehog genes regulate the development of bones and respiratory organs. He also demonstrated how these genes might be regulated artificially. This was a very important finding, as it provides insights into how genes regulate the development of organs.

r. **For the first time**, Dr. Srivastava purified and characterized the human homolog of AAT and ASPT enzymes, which is the basic clinical marker in all infections, as well as the major marker of liver function tests.

s. **For the first time**, Dr. Srivastava demonstrated the co-ordination of AAT and ASPT enzymes in the production of energy through the amino acids after aerobic respiration.

t. **For the first time,** Dr. Srivastava showed that, according to metabolic demand of the body, AAT and ASPT genes synthesized additional forms of its isoform to cope up with the extra energy demand and function as an “on” and off” switch.

B. Publications from GIOSTAR

The following publications demonstrate Dr Anand Srivastava’s advances in field of stem cell therapies. These studies were conducted in conjunction with some of the leading research institutions in the world.

1. Publications from The Salk Institute for Biological Studies, La Jolla, California, USA

The following publications signify the use of stem cells in blood and neural diseases:

a. Basak GW, Yasukawa S, Alfaro A, Halligan S, **Srivastava AS**, Minev B, Carrier E. Human embryonic stem cells hemangioblast express HLA-antigens. J Transl. Med., 7:27-36; 2009. https://translational-medicine.biomedcentral.com/articles/10.1186/1479-5876-7-27

b. Grzegorz Wladyslaw Basak, **Srivastava AS**, Rakesh Malhotra, Ewa Carrier. Multiple Myeloma Bone Marrow Niche. Curren. Pharm. Biotech, 10:345-6, 2009. https://www.ncbi.nlm.nih.gov/pubmed/19355944

c. **Srivastava AS**, Malhotra R, Jason Sharp and Berggren T. Potentials of ES Cell therapy in Neurodegenerative Diseases. Curren. Pharm. Design, 14:3873-9; 2008. https://medcraveonline.com/JSRT/JSRT-03-00095

d. Mahmood A, Pandaya H, Rajasekar S, Patel D and Srivastava AS Cardiovascular Diseases: Recent Developments in Regenerative Medicine. J Stem Cell Res Ther (2017), 3(2): 00095. https://medcraveonline.com/JSRT/JSRT-02-00077.php

e. Mahmood A, Srivastava A, Srivastava S, Pandaya H, Khokhani N, Patel D and Mishra R. Role of Cell Based Approaches in Cancer Immunotherapy. J Stem Cell Res Ther (2017), 2(5): 00077. https://medcraveonline.com/JSRT/JSRT-02-00057.php

f. Mishra T, Sarswat A, Mishra K, **Srivastava AS**. Inflammatory Bowel diseases: Current Therapeutic approaches and potential of using stem cells. J Stem Cell Res Ther (2017), 2 (2) 00057. https://medcraveonline.com/JSRT/JSRT-02-00057.php

g. Devang M. Patel, Jainy Shah, and **Anand S. Srivastava** Therapeutic potential of mesenchymal stem cells in regenerative medicine. Stem Cells Int. 2013. Volume 2013, Article ID 496218, 15 pages. https://www.hindawi.com/journals/sci/2013/496218/

h. Dadheech N, **Srivastava A**, Belani M, Gupta S, Pal R, Bhonde RR, Srivastava AS, Gupta S. Basal expression of pluripotency-associated genes can contribute to stemness property and differentiation potential. Stem Cells Dev. 2013 Jun 15;22(12):1802-17. https://www.ncbi.nlm.nih.gov/pubmed/23343006

i. **Srivastava AS**, Stem cells., Curr Top Med Chem.;11:1591, 2011. https://benthamscience.com/journals/current-topics-in-medicinal-chemistry/volume/11/issue/13/

j. Dhawan P, Ahmad R, **Srivastava AS**, Singh AB., Cancer stem cells and colorectal cancer: an overview. Curr Top Med Chem. 11:1592-8, 2011. https://www.ncbi.nlm.nih.gov/pubmed/21446911

2. Publications from Sanford Burnham Prebys Medical Discovery Institute, La Jolla, California, USA

The following original research article signifies the patients with congenital disorder of glycosylation (CDG), type Ib (MPI-CDG or CDG-Ib) have mutations in phosphomannose isomerase (MPI) that impair glycosylation and lead to stunted growth, liver dysfunction, coagulopathy, hypoglycemia, and intestinal abnormalities.

This article demonstrates that disturbing mannose metabolic flux in mice, especially during embryonic development, induces a highly specific, unanticipated pathological state. It is unknown whether mannose is harmful to human fetuses during gestation; however, mothers who are at risk for having MPI-CDG children and who consume mannose during pregnancy hoping to benefit an affected fetus in utero should be cautious.

a. Sharma V, Nayak J, DeRossi C, Charbono A, Ichikawa M, Ng BG, Grajales-Esquivel E, **Srivastava A**, Wang L, He P, Scott DA, Russell J, Contreras E, Guess CM, Krajewski S, Del Rio-Tsonis K, Freeze HH. Mannose supplements induce embryonic lethality and blindness in phosphomannose isomerase hypomorphic mice. FASEB J. 2014 Apr;28(4):1854-69.
http://europepmc.org/articles/PMC3963023/

3. Publications from University of California Los Angeles (UCLA) , California, USA

a. Embryonic stem cells form the cancerous cells if transplanted. We demonstrate that if mitochondria is well developed and using predominantly oxygen for energy production, formation of tumor by ES cells may be controlled. This paper gives an idea to use ES cells safely for stem cell therapy.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4374603/

b. Sudip Mandal, Anne Lindgren, **Anand Srivastava** and Utpal Banerjee. Role of mitochondria in self-renewal, early differentiation and tumorigenicity of pluripotent stem cell. Stem Cells, 29:486-95, 2011.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4374603/

4. Publication from University of California Irvine, California, USA

a. **Anand S. Srivastava**, Rangnath Mishra, Sharmeela Kausal, Dharam P. Chauhan and Ewa Carrier; Prospects of Embryonic Stem Cells in treatment of Hematopoietic Disorders. Curren. Pharm. Biotech. 8: 51-56, 2007. (**Deals with the approaches to treat blood related diseases**).
https://www.ncbi.nlm.nih.gov/pubmed/17979728

5. Publications from Moores Cancer Center at UC San Diego Health , La Jolla, California

We have reported several first reports that signify the possibilities of using stem cells in blood related diseases, neural related diseases and gene therapy. These original and review articles provided scientists with the initial ideas that gene therapy and stem cells approaches may help in development of clinical treatments for several blood, brain and autoimmune diseases.

a. **Anand S. Srivastava**, Elena Nedelcu, Babak Esmaeli-Azad, Rangnath Mishra and Ewa Carrier; Thrombopoietin Enhances Generation of CD 34+ Cells from Human Embryonic Stem Cells. Stem Cells, 25:1456-61, 2007. (**Showed first time that embryonic stem cells can be used to produce blood stem cells**)
https://www.ncbi.nlm.nih.gov/pubmed/17379761

b. **Anand S. Srivastava**, Dharam Chauhan, Zong Ling Feng, Hyun S Kim and Ewa Carrier; Transplantation of embryonic stem cell in CDIL10-/- KO mouse, an animal model of colitis, antagonizes the manifestation of Crohn's Disease. BBRC 361:953-959, 2007. (**First report to use stem cells in treatment of Crohn's disease, which is a kind of autoimmune diseases**)

c. **Anand S. Srivastava**, Steve Shenouda, Rangnath Mishra and Ewa Carrier; Transplanted Embryonic Stem cells Successfully Survive and Proliferate in Brain and Migrate to Damaged Regions of the Brain. Stem Cells, 24:1689-94, 2006. (**First report to show that stem cells may treat damaged brain**)
https://www.ncbi.nlm.nih.gov/pubmed/16574752

d. **Anand S. Srivastava**, Sharmeela Kaushal, Rangnath Mishra, Thomas A. Lane and Ewa Carrier; Dexamethasone facilitates erythropoiesis in murine embryonic stem cell differentiating into hematopoietic cells in vitro. BBRC, 346:508-16, 2006. (**First report to show that dexamethasone may enhance the blood progenitor cells and give an idea to produce blood cells in lab**).
https://www.ncbi.nlm.nih.gov/pubmed/16764825

e. Marta R., Mara G., **Srivastava A.S**., Matthew, C. W., Kilian S., Carrier E., and Zanetti M.; Immunity over tolerance targeting fetal liver B cells. Vaccine, 23:4273-82, 2005. (**First report to program a developing fetus in mother uterus**).

f. Feng Z, **Srivastava AS**, Mishra R, Carrier E., A regulatory role of Wnt signaling pathway in the hematopoietic differentiation of murine embryonic stem cells. Biochem. Biophys. Res. Commun., 324:1333-9, 2004. (**Showed the significance of Wnt signaling pathway in formation of blood cells**).
https://www.ncbi.nlm.nih.gov/pubmed/15504360

g. **Srivastava A.S**., Chauhan, D.P. and Carrier E.; In utero detection of T7 phage in the fetal tissues after systemic administration to pregnant mice. Biotechniques, 37:81-83,

2004. (**Targeting the fetus through maternal circulation, which give an idea for development of tissue target gene delivery to a fetus to treat genetic diseases**). https://www.ncbi.nlm.nih.gov/pubmed/15283204

h. **Srivastava A.S.**, Kaido T., Carrier E.; Immunological factors that affect the in vivo fate of T7 phage in the mouse. J of Virol. Meth., 115:99-104, 2004. (**Showed first time the way mammalian immune system acts on the T7 phage virus. Which gives an idea to use viral vector effectively for gene delivery**). https://www.ncbi.nlm.nih.gov/pubmed/14656466

i. **Srivastava A.S**, G. Radhakrishna Pillai, Dharam P. Chauhan and Ewa Carrier; Induction of apoptosis in human lung cancer cells by dietary Curcumin. Cancer letters, 208:163-170, 2004. (**Significance of Turmeric powder on the lung cancer gene expression. This shows that Turmeric may be used to treat the lung cancer**). https://www.ncbi.nlm.nih.gov/pubmed/15142674

j. M. E. Moustafa`, **A. S. Srivastava**, E. Nedelcu, S. Shenouda and E. Carrier; Chimerism and tolerance post in utero transplantation with ontogenically different sources of stem cells. Transplantation, 78:1274-1282, 2004. (**Shows first time the use of different sources of stem cells in formation of chimerism**). https://www.researchgate.net/publication/246118325_Chimerism_and_tolerance_post_in_utero_transplantation_with_ontogenically_different_sources_of_stem_cells

k. **A.S. Srivastava**, M. E. Moustafa, S. Shenouda, D. P. Chauhan and E. Carrier; In utero gene therapy: prospect and future. Curren. Pharm. Des., 10:3663-72, 2004. (**Signifies the possibility of gene therapy in genetic diseases**). https://www.ncbi.nlm.nih.gov/pubmed/15579062

l. Sefrioui H, Donahue J, Gilpin EA, **Srivastava AS**, Carrier E. Tolerance and immunity following in utero transplantation of allogeneic fetal liver cells: the cytokine shift. Cell Transplant. 2003;12(1):75-82. (**First report to show the tolerance and immunity after transplanting the fetal liver cells**). https://www.ncbi.nlm.nih.gov/pubmed/12693667

m. Sefrioui H, Donahue J, **Srivastava AS**, Gilpin E, Lee TH, Carrier E. Alloreactivity following in utero transplantation of cytokine-stimulated hematopoietic stem cells: the role of recipient CD4(-) cells. Exp Hematol. 2002 Jun;30(6):617-24. (**First report to show the behaviour of blood stem cells after transplant in a mammalian model**). https://www.ncbi.nlm.nih.gov/pubmed/12063030