

Faculty Details

Name: Prof. Jagan M.R. Pongubala

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Area Of Research: Molecular Genetics, Developmental Immunology, Gene Regulation and Cancer Immunology

Faculty Details

RESEARCH INTERESTS:

Hematopoiesis represents a leading developmental model system for the analysis of gene regulatory networks that dictate cellular development. During hematopoiesis, stem cells (HSCs) progressively undergo lineage restriction and generate a variety of lineage-specific progenitors that ultimately differentiate into mature cell types of the blood. The first step in differentiation involves the loss of self-renewing capacity of HSC, which leads to the generation of the multipotent progenitor, MPP. Our recent studies and work of other research groups provide evidence that differentiation of MPPs involves the selective activation of lineage-specific genes and silencing of lineage inappropriate genes. We have reported that Ebf1 can promote the B lineage-specific genes and possesses the unique ability to 'rescue' the developmental defects associated with the loss of PU.1, a critical factor for B cell generation. Hence, Ebf1 occupies a unique position within the hierarchy of regulatory elements required for B cell specification and commitment (see figure below). Thus, aberrant expression of primary lineage determinant, Ebf1 and it's a downstream factor, Pax5, leads to a block in differentiation, enabling the progenitors to undergo prolonged proliferation, thereby leading to cancer.

Figure. Upper panel; Schematic representation of the hierarchy of lineage-restricted hematopoietic progenitors leading to the development of lymphoid and myeloid lineages. Lower panel; Regulatory circuit that dictates B cell fate choice. This circuit is suggested to operate during the transition from an LMPP to a pro-B cell and may involve ELPs and CLPs as obligate intermediates. EBF1 antagonizes alternate cell fate options by interfering with the expression or function of alternate lineage genes. Importantly, EBF activates early B lineage genes, including the secondary B cell fate determinant, Pax5.

Our current research aims to establish gene regulatory networks that dictate B cell fate commitment and to understand the molecular basis of leukemogenesis. Areas of major interest include discovering transcription factors and miRNAs that control cell fate choice, mechanisms that regulate the lineage-specific gene expression, determine the novel regulatory molecules by gene perturbation and/or editing approaches. Complementary to our research goals, we are developing strategies to model higher-order chromatin structure and organization within the nuclear space and real-time analysis of transcription at a single-gene level in living cells at a high spatiotemporal resolution. We use a diverse set of tools – high-throughput molecular and biochemical approaches, high-end computing, live-cell imaging, and genetic perturbations to decipher the functions of transcription factors and non-coding regulatory elements. Our research has broad implications for understanding the regulation of lineage-specific gene expression program, crucial to the development and function of B and T lymphoid cells.

Current Ph.D. students:

Anurupa Devi., M.Tech., Currently working as an exchange graduate student at the Yale University

Anubhooti S., M.Tech, Working on collaboration project at TIFR -Hyderabad

Priyanka K Narayan., M.Sc., University of Hyderabad

Arpita Prusty., M.Sc., Currently working as an exchange graduate student at the University of California at San Diego (UCSD)

Ashok Kumar., M.Sc., University of Hyderabad

Nidhi Singh., M.Sc., University of Hyderabad

Shravya Lakshmi., M.Sc. University of Hyderabad

Former Ph.D. Students:

Dr. Ravi Boya; Currently working at the University of Pennsylvania

Dr. Sameena Nikhat; Currently present in Northern Ireland

Notice Board

No Records Available

Students And Project Trainees

Students/Projects Trainees

Name	Joined As	Mail	Contact
Nidhi Singh	Research Scholar	---	---
Ashok Kumar	Research Scholar	---	---
Arpita Prusty	Research Scholar	---	---
Priyanka K Narayan	Research Scholar	---	---
Anurupa Devi	Research Scholar	---	---
Anubhooti S	Research Scholar	---	---

Publications

18 Helen Beilinson, Rebecca Glynn, Anurupa Yadavalli, Jianxiong Xiao, Elizabeth Corbett, Huseyin Saribasak, Rahul Arya, Charline Miot, Anamika Bhattacharyya, Jessica Jones, Jagan Pongubala, Craig Bassing, and David Schatz. (2021) , The RAG1 N-terminal region regulates the efficiency and pathways of synapsis for V(D)J recombination , Journal of Exp. Med., „DOI is 10.1084/jem.20210250, IF - 14.5.

- 17 Jagan Pongubala and Cornelis Murre (2021) , Spatial organization of chromatin: Transcriptional control of immune cell development , *Frontiers in Immunology*, ,,2021.633825, IF - 7.5.
- 16 Nikhat, S., Yadavalli, AD., Prusty, A., Narayan, PK., Paldodeti, D., Murre, C., and Pongubala, JMR (2021) , A regulatory network of microRNAs confers lineage commitment during early developmental trajectories of early B and T lymphocytes , *Proc. Natl. Acad. Sci. (USA)*, ,,1-12 IF - 11.3.
- 15 Boya, R., Yadavalli AD, Nikhat, S, Kurukuti, S., Palakodeti, D., and Pongubala, JMR. (2017) , Developmentally regulated higher-order chromatin interactions orchestrate B cell fate commitment , *Nucleic Acids Research*, ,45,,11070 IF - 17.5.
- 14 Laslo, P*., Pongubala, JMR*., Lancki, DW., and Singh, H. (2008) , Gene regulatory networks directing myeloid and lymphoid cell fates within the immune system. , *Seminars in Immunology*, ,20,,228-235 IF - 7.5.
- 13 Pongubala, JMR., Northrup, DL., Lancki, DW., Medina, KL., Treiber, T., Bertolino, E., Thomas, M., Grosschedl, R., Allman, D. and Singh, H. (2008) , EBF restricts alternate lineage options and promotes B cell fate commitment independently of Pax5 , *Nature Immunology*, ,9,,203-215 IF - 25.6.
- 12 Johnson, K., Hashimshony, T., Sawai, CM., Pongubala, JMR., Skok, JA., Aifantis, I. and Singh, H. (2008) , Regulation of immunoglobulin light-chain recombination by the transcription factor IRF-4 and the attenuation of interleukin-7 signaling. , *Immunity*, ,28,,335-345 IF - 31.7.
- 11 Singh, H., and Pongubala, JMR. (2006) , Gene regulatory networks and the determination of lymphoid cell fates. , *Current Opinion in Immunology*, ,18,,116 IF - 7.6.
- 10 Singh, H., Medina, KL., and Pongubala, JMR. (2005) , Gene Regulatory Networks Special Feature: Contingent gene regulatory networks and B cell fate specification. , *Proc. Natl. Acad. Sci. (USA)*, ,102,,4949-4953 IF - 11.3.
- 9 Medina, K., Pongubala, JMR., Reddy, KL., Lancki, DW., DeKoter, R., Kieslinger, M., Grosschedl, R., and Singh, H. (2004) , Defining a regulatory network for specification of the B cell fate. , *Developmental Cell*, ,4,,607-617 IF - 12.2.
- 8 Escalante, CR., Brass, AL., Pongubala, JMR., Shatova, E., Shen, L., Singh, H., and Aggarwal AK. (2002) , Crystal structure of PU.1/IRF-4/DNA ternary complex. , *Molecular Cell*, ,10,,1097-1105 IF - 17.9.
- 7 Rieske, P., and Pongubala, JMR. (2001) , AKT induces transcriptional activity of PU.1 through phosphorylation-mediated modifications within its transactivation domain. , *Journal of Biological Chemistry*, ,11,,8460-8468 IF - 5.1.
- 6 Fisher, RC., Olson, MC., Pongubala, JMR., Perkel, JM., Atchison, ML., Scott, EW., and Simon, MC. (1998) , Normal myeloid development requires both the glutamine rich transactivation domain and the PEST region of transcription factor PU.1 but not the potent acidic transactivation domain. , *Molecular and Cellular Biology*, ,18,,4347-4357 IF - 4.2.
- 5 Pongubala, JMR., and Atchison, ML. (1997) , PU.1 can participate in an active enhancer complex without its transcriptional activation domain. , *Proc. Natl. Acad. Sci. (USA)*, ,94,,127-132 IF - 11.3.

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- 3 Pongubala, JMR., Van Beveren, C., Nagulapalli, S., Klemsz, MJ., McKercher, SR., Maki, RA., and Atchison, ML. (1993) , Effect of PU.1 phosphorylation on interaction with NF-EM5 and transcriptional activation. , Science, ,259,,1622-1625 IF - 41.8.
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- 1 Pongubala, JMR., and Atchison, ML. (1991) , Functional characterization of the developmentally controlled immunoglobulin kappa 3\'-enhancer; regulation by Id, a repressor of helix-loop-helix transcription factors. , Molecular and Cellular Biology, ,11,,1041-1047 IF - 4.2.

Projects

Title	Year	Duration	Amount(In Lakhs)	PI/I
2. Cis-regulatory configuration controlling B-lineage gene expression Jagan Pongubala	2020	3	700000000000	
1. Regulatory functions of microRNAs during early lymphoid lineage differentiation 570000000000 Jagan Pongubala	2019	3		

Open Positions

We are actively looking to recruit students with an excellent background in basic sciences or computational biology.

We welcome outstanding students with a life sciences background including; Cell Biology, Immunology, Development Biology, Molecular Biology, and Biotechnology. Students will have an opportunity to select a project from a wide range of topics in the thrust area of transcription regulation, gene regulatory networks, developmental immunology, and cancer biology. If interested please send an email with your CV at jpsl@uohyd.ernet.in.

We are hiring candidates with excellent experience in computational biology, and mathematics to join our team. To apply, please send an email describing research interests, career goals, and a copy of CV.