Finding expressed genes and novel phyto-compounds as ligands from schizophrenic convergent genomic and pharmacological evidence of PI3K/GSK3 signaling alterations in neurons
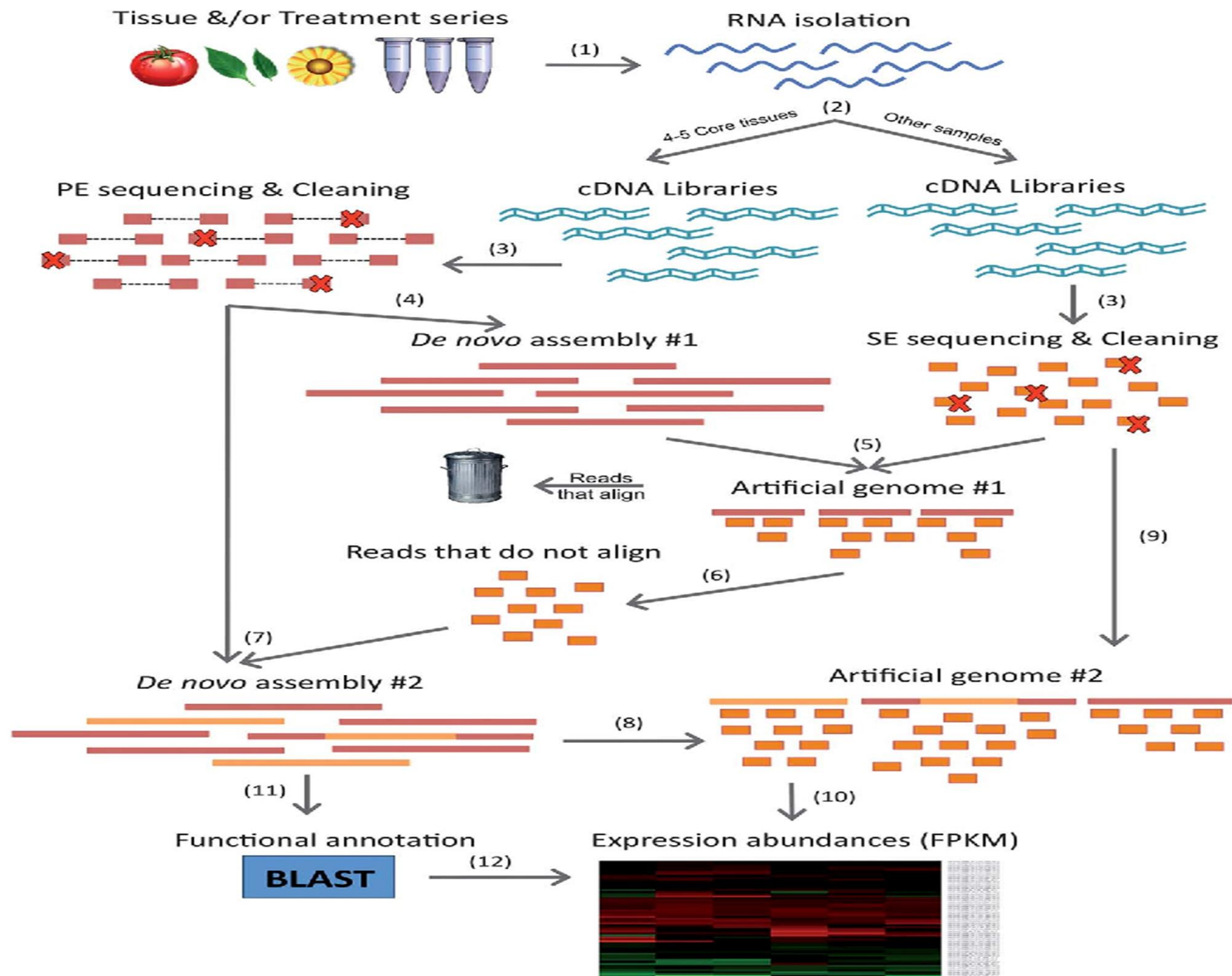
Presented by

Dr. Preenon Bagchi

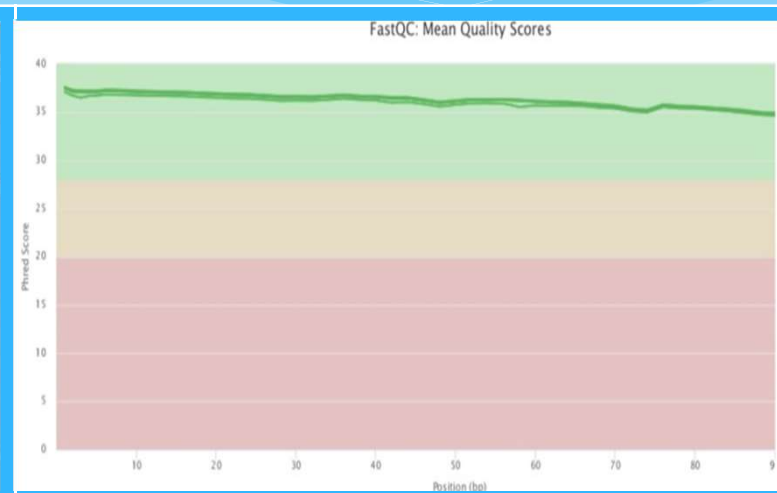**Institute of Biosciences & Technology, MGM University**

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Data retrieval

* Schizophrenia RNA-seq data SRR15629349, SRR15629350, SRR15629351 and SRR15629352 were retrieved from SRA database.

* Work by Stertz L *et al.,* "Convergent genomic and pharmacological evidence of PI3K/GSK3 signaling alterations in neurons from schizophrenia patients.", *Neuropsychopharmacology,* 2021 Feb;46(3):673-682
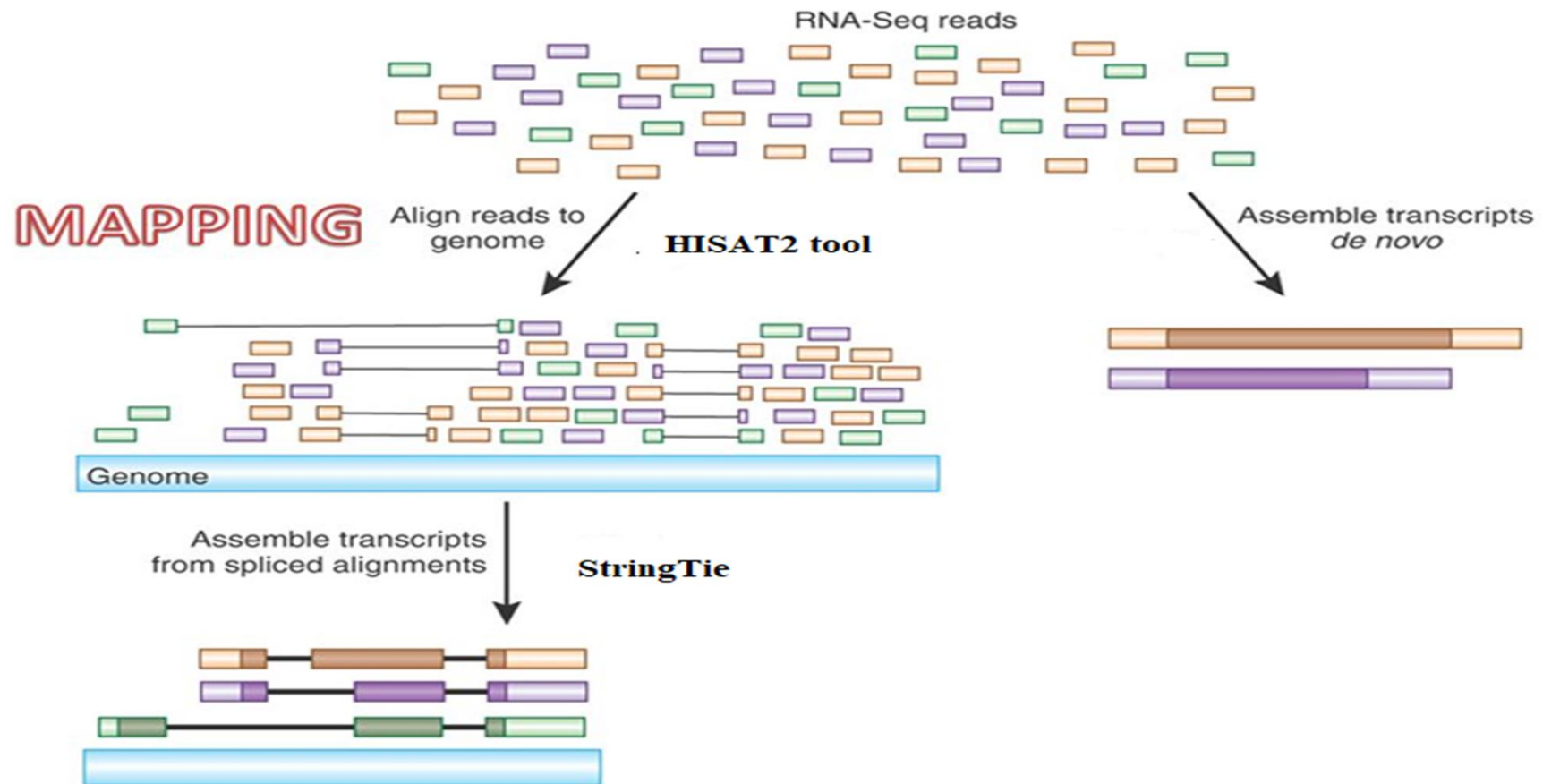
Quality checking of the sequences
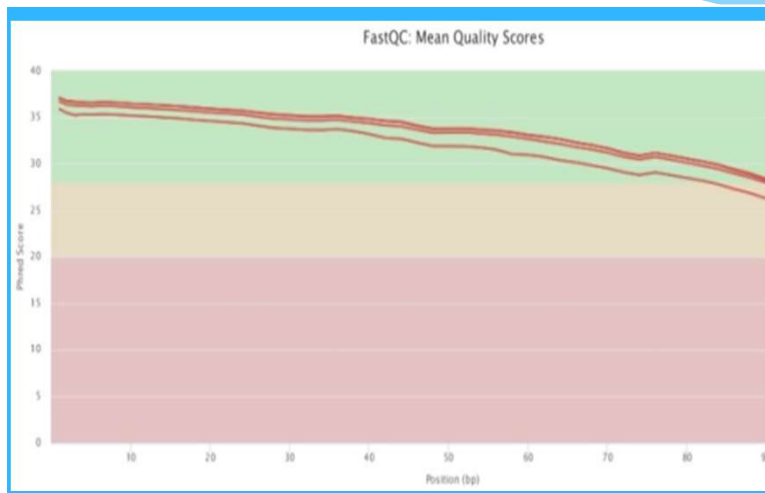

| Raw sequence quality | Sequence quality after trimming |

Sequence quality was checked before and after trimming. This was done by tool FASTQC.

- The sequences were mapped with human reference genome using HISAT2 tool
- Transcriptomes were generated with Stringtie
- Transcriptome database was made by using tool Stringtie - Merge
- Next, GFFcompare annotated the transcripts of our newly created transcriptome to make us known the relationship of each transcript to the human RefSeq reference
- Further, using FeatureCounts tool the reads aligning in exons of our GFFCompare generated transcriptome database was counted
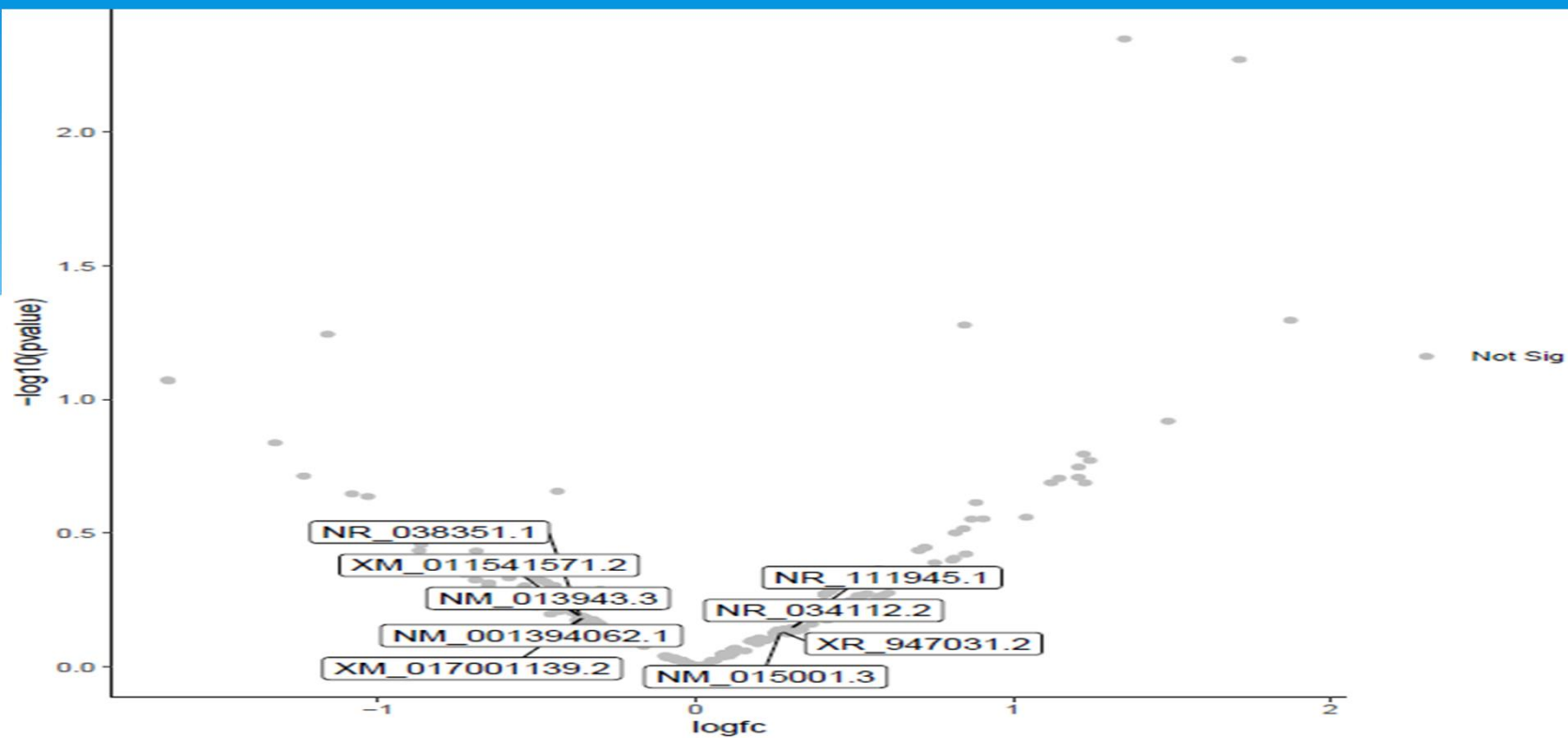
➤ DESeq tool was used to identify the expressed genes.
➤ NR_111945.1, NR_034112.2, XR_947031.2 and NM_015001.3 which are towards the right of the volcano plot are the most up-regulated genes and NM_001039211.3, NR_038351.1, XM_011541571.2, NM_013943.3, XM_017001139.2 and NM_001394062.1 are towards the left are the most down-regulated genes
➤ From the genes above, NR_038351.1 is the most significant gene since it is on the topmost amongst the genes.

High-Throughput Screening (HTS)

* Homology modeling of the selected above receptors was done.
* Phyto-compounds from Ayurvedic Medicinal plants *Withania sominefera, Melisa officinalis, Piper methysticum, Veleriana officinalis* and *Hypericum perforatum* are traditionally used to treat many diseases are considered here.
* As per Lipinski's rule of five [ADME (Adsorption, distribution and metabolism extraction)] we checked the drug likeliness of the above phyto-compounds.
* As per docking result it is seen that the phytocompounds Lutolin, Kaemferol, Ginkolide A, Ascorbic asid, Tetrahydroyangonin, Matteacinol, 5-hydroxy-4-7-dimethoxy, Tetrahydro yangonin, D-Allose and Azetidine docks with all the receptors.
* Hence these compounds can be successfully considered as ligands for the receptors on further validation using in-vitro and in-vivo studies.

Reference

* Andreasen, N. C., & Flaum, M. (1991). Schizophrenia: the characteristic symptoms. *Schizophrenia bulletin*, 17(1), 27-49.

* Andreasen, N. C. (1982). Negative symptoms in schizophrenia: definition and reliability. *Archives of general psychiatry*, 39(7), 784-788.

* Chapman, J. (1966). The early symptoms of schizophrenia. *The British Journal of Psychiatry*, 112(484), 225-251.

* Crow, T. J. (1981). Positive and negative schizophrenia symptoms and the role of dopamine. *The British Journal of Psychiatry*, 139(3), 251-254.

* Kane, J. M., & Marder, S. R. (1993). Psychopharmacologic treatment of schizophrenia. *Schizophrenia bulletin*, 19(2), 287-302.

* Kahn RS, Sommer IE, Murray RM, Meyer-Lindenberg A, Weinberger DR, Cannon TD, O'Donovan M, Correll CU, Kane JM, Van Os J &Insel TR 2015, "Schizophrenia", Nature Reviews Disease Primers, 1, 15067. https://doi.org/10.1038/nrdp.2015.67

* Bagchi P, Kar A and Somashekar R, 2015, "Ayur-Informatics: Finding Best Ligands For Ampa Receptor Implicated In Schizophrenia From Indian Ayurvedic Herbs", The International Journal of Psychosocial and Cultural Genomics, Consciousness & Health Research, 2(1):37-41

* Ramu MG, Venktaram BS, 1992, "A Controlled Study of Ayurvedic Treatment in the Acutely ill Patients with Schizophrenia (Unmada) - Rationale and Results", NIMHANS Journal, 10(1):1-16

* Shilpa S, Venkatesha Murthy CG. 2011, "Understanding personality from Ayurvedic perspective for psychological assessment: A case". *Ayu.*;32(1):12-19. doi:10.4103/0974-8520.85716