Week 2 – Previously found genes and other biological signatures

1. **ASCL1** *(Transcription Factor)*
   ASCL1 is a basic helix-loop-helix (bHLH) transcription factor that acts as a pioneer factor in neuronal reprogramming. It binds to closed chromatin regions, initiating the activation of neuronal gene expression programs. ASCL1 alone can induce neuronal features in fibroblasts, and its efficiency is enhanced when combined with other factors like BRN2 and MYT1L.

2. **BRN2 (POU3F2)** *(Transcription Factor)*
   BRN2 is a POU-domain transcription factor that promotes neuronal differentiation. It works synergistically with ASCL1 and MYT1L to enhance the maturation of induced neurons, facilitating the development of functional neuronal properties.

3. **MYT1L** *(Transcription Factor)*
   MYT1L is a zinc finger transcription factor that reinforces neuronal identity by repressing non-neuronal gene expression. It suppresses genes associated with fibroblast and glial identities, thereby stabilizing the neuronal phenotype during reprogramming.

4. **NEUROD1** *(Transcription Factor)*
   NEUROD1 is a bHLH transcription factor that promotes late-stage neuronal differentiation. It enhances the functional maturation of induced neurons and is often used in combination with other neurogenic factors to improve reprogramming outcomes.

5. **NEUROD2** *(Transcription Factor)*
   Similar to NEUROD1, NEUROD2 supports the progression of neuronal identity and is associated with increased neuronal functionality when overexpressed. It contributes to the development of mature neuronal characteristics.

6. **NGN2 (Neurogenin 2)** *(Transcription Factor)*
   NGN2 is a potent neurogenic bHLH transcription factor capable of independently driving the conversion of fibroblasts into neurons. It activates a cascade of neuronal genes and is often used in both direct reprogramming and differentiation protocols to generate excitatory neurons.

7. **miR-124** *(MicroRNA)*
   miR-124 is a neuron-specific microRNA that promotes neuronal identity by repressing anti-neuronal genes and facilitating chromatin remodeling. It targets components of chromatin remodeling complexes and shifts the cellular gene expression landscape toward a neuronal profile.

8. **miR-9/9*** *(MicroRNA)*
   miR-9 and its complementary strand miR-9* act synergistically with miR-124 to repress genes that maintain non-neuronal identity. They promote chromatin states conducive to neuronal gene expression and are crucial for the efficient reprogramming of fibroblasts into neurons.

9. **LMX1A** *(Transcription Factor)*
   LMX1A is involved in the specification of midbrain dopaminergic neurons. It activates dopaminergic-specific genes when co-expressed with factors like NURR1 and FOXA2, guiding fibroblasts toward a dopaminergic neuronal fate.

10. **NURR1 (NR4A2)** *(Transcription Factor)*
    NURR1 is critical for the development and maintenance of dopaminergic neurons. It promotes the expression of dopamine-related enzymes and transporters, contributing to the functional properties of dopaminergic neurons derived from fibroblasts.

11. **FOXA2** *(Transcription Factor)*
    FOXA2 facilitates the specification of the dopaminergic neuron lineage by modulating the transcriptional environment early in reprogramming. It works in concert with LMX1A and NURR1 to induce dopaminergic characteristics in reprogrammed cells.

12. **LHX3** *(Transcription Factor)*
    LHX3 is involved in specifying motor neuron identity. It works in combination with other factors like ISL1 to direct fibroblasts toward a motor neuron fate during reprogramming.

13. **HB9 (MNX1)** *(Transcription Factor)*
    HB9 is a motor neuron-specific transcription factor that plays a role in the development of spinal motor neurons. It is used to generate this subtype during reprogramming by promoting motor neuron-specific gene expression.

14. **ISL1** *(Transcription Factor)*
    ISL1 is essential for motor neuron development and is used to specify motor neuron identity in reprogramming cocktails. It collaborates with LHX3 and HB9 to induce motor neuron characteristics in fibroblasts.

15. **SOX5** *(Transcription Factor)*
    SOX5 regulates cortical neuron identity. When expressed with other cortical-specific factors, it helps guide fibroblasts into a cortical neuronal lineage by promoting the expression of cortical neuron-specific genes.

16. **FEZF2** *(Transcription Factor)*
    FEZF2 promotes the development of deep-layer cortical neurons and helps maintain their identity. It is involved in specifying subcortical projection neurons during cortical development and reprogramming.

17. **CTIP2 (BCL11B)** *(Transcription Factor)*
    CTIP2 functions in the development of subcortical projection neurons and is involved in the specification of cortical neuron subtypes. It contributes to the establishment of neuronal circuits by promoting the expression of genes associated with cortical projection neurons.

18. **TBR1** *(Transcription Factor)*
    TBR1 is required for the development of glutamatergic cortical neurons. It supports the maturation and identity of upper-layer cortical neurons by regulating genes involved in neuronal differentiation and connectivity.

19. **DNMT3A** *(Gene/Protein – DNA Methyltransferase)*
    DNMT3A encodes a protein that adds methyl groups to DNA, helping establish epigenetic marks needed to suppress fibroblast-specific genes and activate neuronal programs. It plays a role in the epigenetic remodeling necessary for neuronal reprogramming.

20. **EGR1** *(Transcription Factor)*
    EGR1 facilitates chromatin remodeling during reprogramming by recruiting enzymes that

remove methylation marks, thereby activating silent neuronal genes. It contributes to the epigenetic changes required for the acquisition of neuronal identity.

21. **TET1** *(Protein – DNA Demethylase)*
    TET1 works to demethylate DNA, allowing repressed neuronal genes to be reactivated. It is often involved downstream of transcription factors like EGR1 and plays a role in the epigenetic reprogramming of fibroblasts into neurons.

22. **CHD5** *(Chromatin Remodeler – Protein)*
    CHD5 is a chromatin remodeler that is upregulated during neuronal reprogramming. It plays a role in modifying chromatin structure to facilitate the activation of neuronal gene expression programs.

23. **BAF Complex (SWI/SNF Complex Components)** *(Protein Complex)*
    The BAF complex is involved in chromatin remodeling during neuronal differentiation. Components like BAF53b replace non-neuronal subunits (e.g., BAF53a) during reprogramming, facilitating the establishment of a neuronal chromatin landscape.

24. **PTBP1 and PTBP2** *(RNA-Binding Proteins)*
    PTBP1 is a repressor of neuronal-specific splicing and is downregulated during reprogramming, while PTBP2 is upregulated. This switch in expression is crucial for the activation of neuronal-specific alternative splicing programs necessary for neuronal function.

25. **REST (RE1-Silencing Transcription Factor)** *(Transcriptional Repressor)*
    REST represses neuronal gene expression in non-neuronal cells. During reprogramming, REST is downregulated, relieving its suppression on neuronal genes and allowing the activation of neuronal programs.

26. **miR-302/367 Cluster** *(MicroRNA Cluster)*
    The miR-302/367 cluster facilitates reprogramming by targeting multiple genes involved in maintaining the fibroblast state. When combined with miR-124 and miR-9/9*, it enhances neuronal lineage conversion by promoting a chromatin environment conducive to neuronal gene expression.

27. **DLX1 and DLX2** *(Transcription Factors)*
    DLX1 and DLX2 are involved in the development of GABAergic interneurons. When co-expressed with miR-9/9*-124 and MYT1L, they guide the conversion of fibroblasts into striatal GABAergic medium spiny neurons by activating subtype-specific gene expression programs.

28. **BCL11B (CTIP2)** *(Transcription Factor)*
    BCL11B, also known as CTIP2, is critical for the development of striatal medium spiny neurons. It works in conjunction with other factors to specify neuronal subtype identity during reprogramming.

29. **RN7SK** *(Small Nuclear RNA)*
    RN7SK is a small nuclear RNA required to activate neuronal lineage genes through changing chromatin accessibility. Its upregulation is part of the sequential steps in silencing fibroblast fate and promoting neuronal identity during reprogramming.

30. **KLF4 and KLF5** *(Transcription Factors)*
    KLF4 and KLF5 are transcription factors associated with maintaining fibroblast identity. Their

silencing is one of the initial steps in reprogramming fibroblasts into neurons, allowing the activation of neuronal gene expression programs.

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