The Role of Hydroxymethylation in Bronchopulmonary Dysplasia

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BPD and EPIGENETICS

→Exposure to noxious stimuli including hyperoxia contribute to bronchopulmonary dysplasia (BPD) in premature neonates

→Hyperoxia leads to epigenetic changes in the developing lung[1]

→DNA ***hydroxymethylation*** through Ten-Eleven Translocation (TET) leads to increased DNA expression[2]

→The role of hydroxymethylation in the development of BPD remains unknown

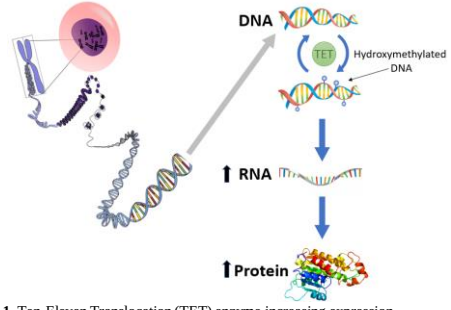
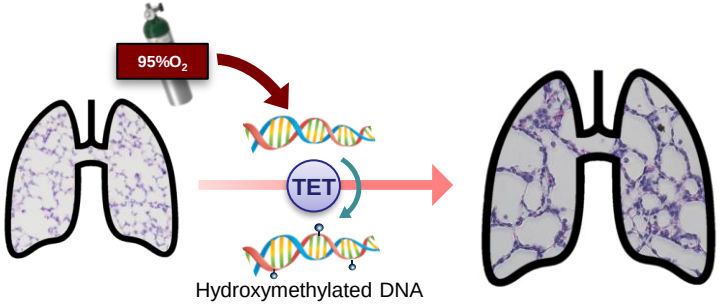


Fig 1. Ten-Eleven Translocation (TET) enzyme increasing expression

HYPOTHESIS



Early exposure of the developing lung to hyperoxia leads to alterations in DNA hydroxymethylation by ten-eleven translocation, and these epigenetic changes contribute to the development of bronchopulmonary dysplasia.

RESULTS and CONCLUSIONS

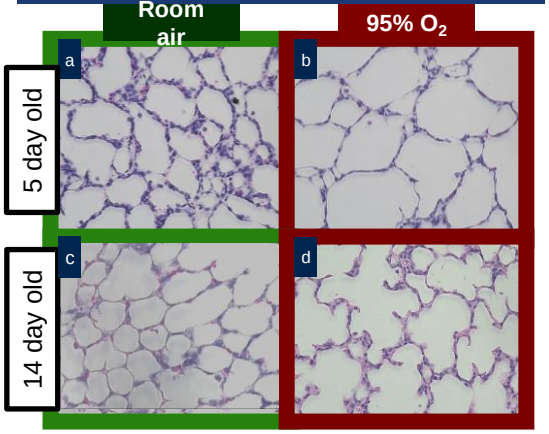


Fig 3: H&E stained lung samples (40x) demonstrating disruption of alveolarization with hyperoxia exposure. (a) 5-day-old 21% O_2 exposed demonstrates normal alveolar development. (b) Larger and fewer alveoli are seen at 5-day-old 95% O_2 exposed animals. (c) Normal alveolar development at 14-day-old in 21% O_2 exposed mice. (d) Continued decreased alveolarization in 14-day-old 95% O_2 exposed mice.

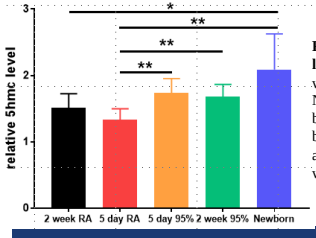


Fig 4: Dot blot analysis of 5hmc levels. The graph shows the genome wide hydroxymethylation level. Notably, there is a significant difference between the levels of 5-hmc at 5-days between RA and 95% O_2 exposed animals and a lesser difference at 2-weeks.

DESIGN and METHODS

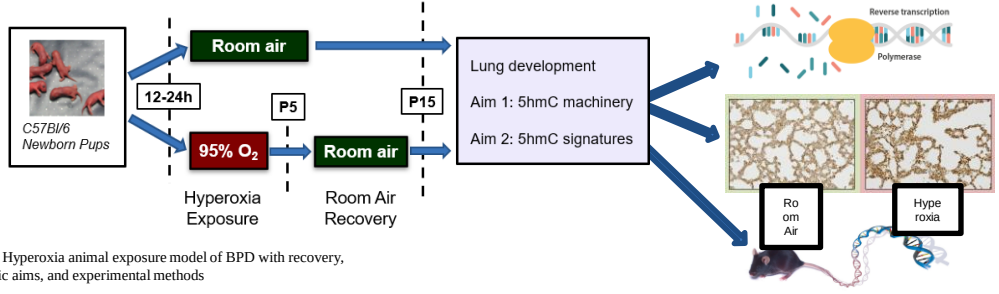


Fig 2: Hyperoxia animal exposure model of BPD with recovery, specific aims, and experimental methods

RT-PCR for TET RNA quantification

Immuno-Histochemistry For TET protein

Genome-wide 5hmc analysis

REFERENCES

1. Oxygen in the neonatal period: Oxidative stress load and epigenetic changes. Lorente-Pozo et al. *Semin Fetal Neonatal Med*. 2020.
2. Conversion of 5-Methylcytosine to 5-Hydroxymethylcytosine in Mammalian DNA by MLL Partner TET1. Tahiliani et al. *Science*. 2009.