Defining the Role of Bromodomain PHD Finger Transcription Factor in the Heart

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BACKGROUND

Proteins that contain bromodomains have recently been associated with multiple diseases including cardiovascular disease. Bromodomains are a conserved family of protein interaction modules that bind to acetylated lysine residues[1]. Bromodomain containing PHD Finger Transcription Factor (*Bptf*) has an important role in remodeling the chromosome to allow for transcription (Figure 1[2]).

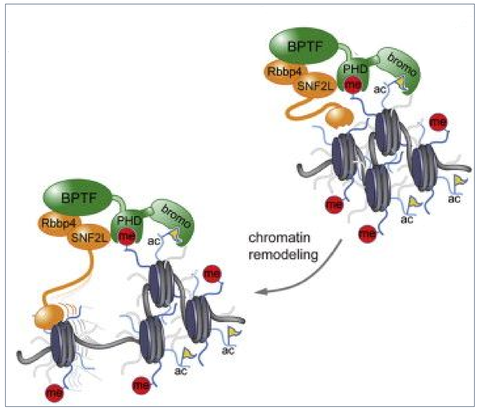

Figure 1. Schematic of *Bptf* on the histone.
The figure shows the role of *Bptf* in chromatin remodeling to allow for transcription. *Bptf* slides the histones over to allow polymerases and other proteins to bind so transcription can start.

OBJECTIVE

To define how *Bptf* affects heart function in mice.

HYPOTHESIS

Deletion of *Bptf* in the murine heart will alter cardiovascular function.

MATERIALS & METHODS

Breeding Strategy: As shown in Figure 2[3].

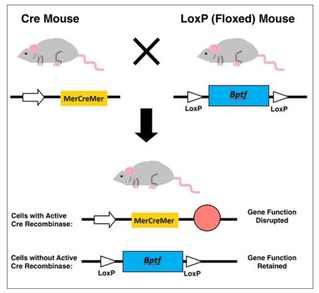

Figure 2. Breeding strategy.
Schematic showing the crossing of *Bptf*$^{flox/flox}$ mice with homozygous alpha myosin heavy chain cre mice in order to achieve the desired genotype of *Bptf*$^{flox/flox\ cre+}$. This also depicts the effect of Tamoxifen on the expressed gene.

Treatment Strategy: As shown in Figure 3.

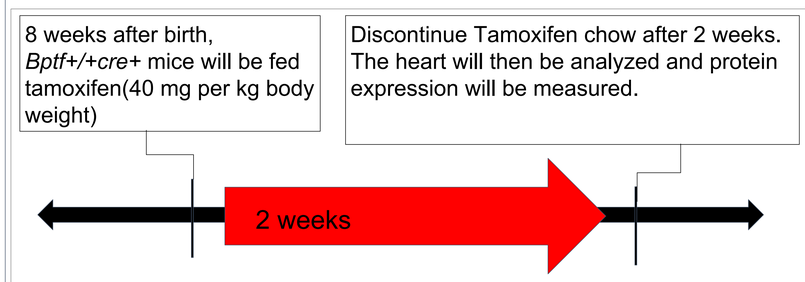

Figure 3. Treatment Strategy.
Schematic showing the projected timeline of the experiment. After feeding the mice tamoxifen for fourteen days, the heart and gene expression of *Bptf* will be analyzed.

METHODS

DNA Isolation was performed on tissue samples from the tails of two month old mice.
PCR was performed to amplify DNA
Gel Electrophoresis was performed to decipher the bands in order to determine the genotype of each mouse.

RESULTS

Genotyping of the litters was performed by DNA extraction from tissue samples followed by PCR. The PCR products were then run on a 2% agarose gel (Figure 4). We are currently genotyping *Bptf*$^{flox/flox\ cre+}$ mice.

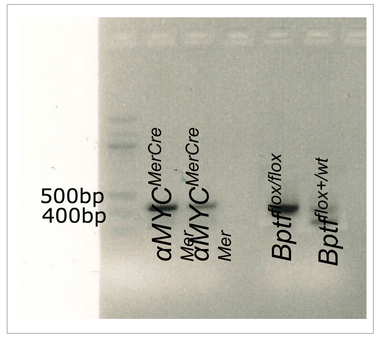

Figure 4. PCR products on polyacrylamide gel.
The results of DNA gel electrophoresis. Mutant alleles (*Bptf*$^{flox/flox}$) show a band at 450 bp, wild type alleles show a band at 350 mp, and heterozygous shows both. Cre transgene alleles show at 450 bp.

FUTURE DIRECTIONS

After the mice have been fed Tamoxifen, deletion of *Bptf* will be confirmed by RTQ PCR and Western Blotting. Echocardiograms will determine how and if heart function is altered in mice with gene deletion, compared to the controls. Further analysis of altered heart function will be measured by performing stress tests. Additionally, examination can be extended to the deletion of *Bptf* in smooth muscle cells via cre transcription into alpha-smooth muscle actin.

REFERENCES

1.Sanchez, R. "The Role of Human Bromodomains in Chromatin Biology and Gene Transcription." *Current Opinion in Drug Discovery & Development*.
2. Ruthenburg, AJ."Recognition of a Mononucleosomal Histone Modification Pattern by BPTF via Multivalent Interactions." *Cell* 145.5 (2011)
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