# DCM Variants

Final Project BIOL 8803F, Fall 2016

## TEAM MEMBERS

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## OVERVIEW

### Scope

Dilated cardiomyopathy (DCM) is a disease of the heart muscle, the heart becomes weaker and its failure can occur. Dilated cardiomyopathy also can lead to heart valve problems, arrhythmias (irregular heartbeats) and blood clots in the heart. Often, cause of dilated cardiomyopathy is not known but up to one-third of the people of those who have it inherit it from their parents. Therefore, it is fundamental to find the mutations that more likely can cause the disease in the members of the same family tree.

### Data

Hiseq Exome sequencing data from 4 patients and 2 controls from the same family tree. Analysis of genetic variants among 6 genes: LMNA, MYBPC3, MYH6, MYH7, SCNSA, TNNT2.

### Results

From our analysis the variants that are more likely to cause the disease:

**chr1 156104248 LMNA**

**chr14 23858232  MYH6**

The first variant was found in all the patients and the second in three of the patients. None of them were found in the controls.

## Methodology

- Search for the genes that are more likely to cause DCM in the same family tree across the literature. This narrowed down the gene pool to

  **LMNA (NM_170707)**

  **MYBPC3 (NM_000256)**

  **MYH6 (NM_002471)**

  **MYH7 (NM_000257)**

  **SCNSA (NM_198056)**

  **TNNT2 (NM_001001430)**

- For each person, perform the variant call analysis and variant recalibration using GATK-HaplotypeCaller. Then, recalibrate the output obtained using GATK-recalibrator.

- For each person, analyze the depth distribution for each exon in all genes. Eliminate the mutations with depth below the lower whisker (cutoff) of the exon they belong. See Plot 1 for an example of depth distribution among the exons and Table 2 for an example of the cutoffs.

- Select the mutations found in at least 3 of the patients and none of the controls as more likely to be pathogenic.

## Limitations

In Table 1 the variants that were found in all patients and only one controls are listed. We recommend to reanalyzed those sites in the controls because they are chances that they may be pathogenic.

## SUPPLEMENTARY MATERIAL

- **Table 1:** Variants found in all patients and one control

| CHR | POSITION | Wild Allele | Mutated Allele | Gene |
|---|---|---|---|---|
| chr1 | 156107534 | C | T | LMNA |
| chr14 | 23861811 | A | G | MYH6 |
| chr14 | 23865885 | G | A | MYH6 |
| chr14 | 23874523 | C | T | MYH6 |
| chr3 | 38622467 | T | C | SCNSA |
| chr3 | 38674712 | T | C | SCNSA |

- **Table 2:** Depth distribution significant values and cutoffs of LMNA in Patient 1

| MEDIAN | 90th_QUANTILE | EXON1 | EXON2 | EXON3 | EXON4 | EXON5 |
|---|---|---|---|---|---|---|
| 33 | 0 | 0 | 106 | 7 | 25 | 23 |

| EXON6 | EXON7 | EXON8 | EXON9 | EXON10 | EXON11 | EXON12 |
|---|---|---|---|---|---|---|
| 20 | 22 | 94 | 56 | 38 | 16 | 0 |

- **Boxplot:** Exon depth distribution plots of MYH6 in Patient 1