

Gene regulation of the Duchenne muscular dystrophy

Clustering results: Complete Linkage

Using Complete Linkage the 107 nontrivial t-invariants are split into 22 t-clusters. The biological meaning of the t-invariants belonging to one t-cluster is given below.

t-cluster 1: t-invariants 40, 41

initiation and up-regulation of the gene *CSNK1A1*, the protein *CSNK1A1* activates *p53*, followed by *p21* transcription, which inhibits *CDK2*

t-cluster 2: t-invariants 38, 39

initiation and down-regulation of the gene *CSNK1A1*, the protein *CSNK1A1* activates in a decreased manner *p53* followed by *p21* transcription, which inhibits *CDK2*

t-cluster 3: t-invariant 34

initiation of dystrophin followed by generation of *DGC* and simulation of DMD by *DGC* loss

t-cluster 4: t-invariants 48, 49, 51, 52, 54, 55, 57, 58

regulated RAP2B downstream pathway, including Ca release, which activates regulated *NFATc*; no transcriptional activity due to deactivation of *NFATc* in cytosol by regulated *CSNK1A1*

t-cluster 5: t-invariants 17, 19, 21, 23, 25, 27, 29, 31

regulated RAP2B downstream pathway, including Ca release, which activates regulated *NFATc*, followed by transcription of *UTRNA*, and deactivation of *NFATc* in nucleus by regulated *CSNK1A1*

t-cluster 6: t-invariants 86 - 89, 92 - 95

regulated RAP2B downstream pathway, including Ca release depending on concentration gradient between Er and cytosol, which activates regulated *NFATc*, followed by *p21* transcription, and deactivation of *NFATc* in nucleus by regulated *CSNK1A1*

t-cluster 7: t-invariants 74 - 77, 80 - 83

regulated RAP2B downstream pathway, including Ca release regulated by calreticulin, which activates regulated *NFATc*, followed by *p21* transcription, and deactivation of *NFATc* in nucleus by regulated *CSNK1A1*

t-cluster 8: t-invariants 16, 18, 20, 22, 24, 26, 28, 30

regulated RAP2B downstream pathway, including Ca release, which activates *NFATc*, followed by transcription of *MYF5*, and deactivation of *NFATc* in nucleus by regulated *CSNK1A1*

t-cluster 9: t-invariant 37

initiation, up/down-regulation of *JNK1*

t-cluster 10: t-invariant 32, 33, 42

DGC downstream pathway, which activates up-regulated *JNK1*, followed by a *c-JUN* phosphorylation dependent *p21* inhibition; regulated transcription of *p21* by *p53* or *NFATc*, respectively

t-cluster 11: t-invariants 50, 53, 56, 59, 96, 97, 98, 99

DGC downstream pathway, which activates regulated *JNK1*; regulated RAP2B downstream pathway, which activates regulated *NFATc*, followed by transcription and no transcriptional activity, respectively, and deactivation of *NFATc* in nucleus by *JNK1*

t-cluster 12: t-invariants 8 - 15, 60 - 73, 78, 79, 84, 85, 90, 91

DGC downstream pathway, which activates regulated *JNK1*; regulated RAP2B downstream pathway, which activates regulated *NFATc*, followed by transcription and no transcriptional activity, respectively, and deactivation of *NFATc* in nucleus by *JNK1*

t-cluster 13: t-invariants 100 - 107

regulated RAP2B downstream pathway, including Ca release, which activates regulated *NFATc*, followed by a transcription of *MLC2*, *aActin*, *ANF*, and deactivation of *NFATc* in nucleus by regulated *CSNK1A1*

t-cluster 14: t-invariant 47

regulated *NFATc* mediates transcription of *MLC2*, *aActin*, and *ANF*, followed by degradation of *NFATc* in nucleus

t-cluster 15: t-invariant 35

initiation and down-regulation of *NFATc*

t-cluster 16: t-invariant 7

regulated *NFATc* mediates transcription of *MYF5*, followed by degradation of *NFATc* in nucleus

t-cluster 17: t-invariants 43, 44

regulated *NFATc* mediates *p21* transcription inhibiting *CDK2*, followed by degradation of *NFATc* in nucleus

t-cluster 18: t-invariant 6

regulated *NFATc* mediates transcription of *UTRNA*, followed by degradation of *NFATc* in nucleus

t-cluster 19: t-invariant 36

initiation, down-regulation and removal of calcineurin

t-cluster 20: t-invariants 5

initiation, up-regulation and degradation of calcineurin

t-cluster 21: t-invariants 4, 45, 46

CDK-dependent RB-E2F cell cycle pathway, resulting in transcription of S-phase genes

t-cluster 22: t-invariants 1, 2, 3

RB-E2F cell cycle pathway, inhibited by CDK2-phosphorylated *E2F*