Docket #: S14-011

mdx/mTR mouse model of Duchenne Muscular Dystrophy

Dr. Helen Blau and colleagues have developed a mouse model that recapitulates both the skeletal muscle and cardiac pathology seen in Duchenne Muscular Dystrophy (DMD) patients. DMD, the most common inherited myopathy of childhood, is a muscle degenerative disease that leads to early death due to cardiorespiratory failure. Although the genetic defect underlying DMD (absence of dystrophin) has been known for more than two decades, there is still no effective treatment or cure. A challenge to therapeutic development has been that the mouse model (mdx) which lacks dystrophin (as humans do) manifests only mild symptoms that primarily affect the skeletal muscles, not the heart, and has a normal lifespan. To overcome this limitation and more faithfully model the clinical symptoms of DMD patients, the inventors generated a dystrophic mouse with shortened telomeres, known as the mdx/mTR mouse. These mice more accurately recapitulate the human disease as evidenced by severe progressive loss of muscle form and function.

Stage of research
The inventors have shown that, like DMD patients, the mdx/mTR mice have severe muscular dystrophy that progressively worsens with age. Furthermore, the mdx/mTR mice develop severe functional cardiac deficits including ventricular dilatation, contractile and conductance dysfunction and accelerated mortality.

Availability of mdx/mTR mice
The mice have been deposited at Jackson Labs, Stock Number 023535. For-profit entities will need to obtain a license from Stanford prior to purchase.

Applications

- Research
    - Elucidate the pathophysiology of DMD

- Therapeutic development to:
  - Restore regenerative properties of dystrophic skeletal muscle
  - Treat cardiorespiratory failure in DMD

Advantages

- Accurately models the skeletal muscle and cardiac pathophysiology seen in DMD patients
- Etiology similar to DMD patients

Publications

- Mourkioti F, Kustan J, Kraft P, Day JW, Zhao MM, Kost-Alimova M, Protopopov A, DePinho RA, Bernstein D, Meeker AK, Blau HM. Role of telomere dysfunction in cardiac failure in Duchenne muscular dystrophy. Nat Cell Biol. 2013 Aug;15(8):895-904. doi: 10.1038/ncb2790. Epub 2013 Jul 7.
- Sacco A, Mourkioti F, Tran R, Choi J, Llewellyn M, Kraft P, Shkreli M, Delp S, Pomerantz JH, Artandi SE, Blau HM. Short telomeres and stem cell exhaustion model Duchenne muscular dystrophy in mdx/mTR mice. Cell. 2010 Dec 23;143(7):1059-71. doi: 10.1016/j.cell.2010.11.039. Epub 2010 Dec 9.

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