Journal of Genetic Syndromes & Gene Therapy
ISSN: 2157-7412

Lu, J Genet Syndr Gene Ther 2013, 4:2
DOI: 10.4172/2157-7412.1000e121

Editorial Open Access

Transgenic Animal Models for Brain 5-HT Deficiency: An Editorial Summary

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Editorial

Animal: Pet-1 KO mice
First Report Year: 2003
Methods: Pet-1 Knock out
Lab: Evan Deneris
Loss of 5-HT Neurons: 80% deficiency of the central 5-HT neurons
Life Span and Body Weight: Survive to adult and normal body weight

Behavior:

- Heightened anxiety-like and aggressive behavior in adults [1].
- Extended and exacerbated period of breathing instability that occurs immediately after birth during which respiratory homeostasis is vulnerable to environmental challenges [2].
- Abnormal maternal behavior which affects offspring survival [3].
- A lack of cognitive deficits and an anxiety phenotype complicated by hypoactivity and defensiveness [4].
- Autoresuscitation responses to hypoxia-induced apnea are delayed in newborn mice [5].
- Altered ventilatory and thermoregulatory control [6].
- Bradycardia (the first 2 postnatal weeks) [7].
- Failed heart rate recovery at early age exposed to episodic anoxia [8].
- Autonomic dysregulation during mild cold stress in the neonatal period [9].

Animal: Lmx1b conditional KO mice

First Report Year: 2006

Methods: Conditional Lmx1b Knock out in pet1-expressing 5-HT neurons.

Labs: Zhou-Feng Chen, Yu-Qiang Ding and Lin Xu.

Loss of 5-HT Neurons: The initial generation of central 5-HT neurons appeared normal (at E11). However, the expression of both 5-HTspecific and non-5-HT-specific markers was lost in these neurons at later stages of development. Almost all central 5-HT neurons failed to survive.

Life Span and Body Weight: Survive to adult; and neonatal: lag in weight gain (because of hypoxia); adulthood: normal body weight.

Behavior:

- Normal locomotor activity [10].
- Neonatal: Frequent and severe apnea and high mortality [11].
- Adulthood: A blunted hypercapnic ventilatory response and impaired cold-induced thermogenesis (impaired shivering and brown adipose tissue activation) [12,13].
- Less sensitive to mechanical stimuli and exhibited enhanced inflammatory pain, the analgesic effect of several antidepressant drugs, including selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), and tricyclic antidepressants, was either abolished or greatly attenuated [14].
- Increase in wakefulness [15].
- Enhanced contextual fear memory [16].

Animal: Tph2 KO mice

First Report Year: 2008 [17]

Methods: Tph2 Knock out

Labs: Katerina Savelieva, Klaus-Peter Lesch, Michael Bader, Gerard Karsenty, Donald M. Kuhn and Yi Rao.

Loss of 5-HT Neurons: Normal central 5-HT neuron formation.

Life Span and Body Weight: Survive to adult, growth retardation [18,19] and persistent leanness [18].

Behavior:

- More extended daytime sleep, suppressed respiration, altered body temperature control, and decreased blood pressure (BP) and heart rate (HR) during nighttime; Tph2 ko females, exhibit impaired maternal care leading to poor survival of their pups [19].
- Exaggerated aggression and decreased anxiety [20].
- A severe low bone mass phenotype affecting axial (vertebrae) and appendicular (long bones) skeleton while bone length and width were unaffected [21].
- Respond to METH in the same manner as wild-type controls, despite showing enhanced drug-induced hyperthermia [22].
- Substantial deficits in numerous validated tests of social interaction and communication; highly repetitive and compulsive behaviors; Newborn mice show delays in the

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Received January 02, 2013; **Accepted** January 05, 2013; **Published** January 07, 2013

Citation: Lu J (2013) Transgenic Animal Models for Brain 5-HT Deficiency: An Editorial Summary. J Genet Syndr Gene Ther 4: e121. doi:10.4172/2157-7412.1000e121

expression of key developmental milestones and their diminished preference for maternal scents over the scent of an unrelated female is a forerunner of more severe socialization deficits that emerge in weanlings and persist into adulthood [23].

- Males did not show a preference between male and female bedding and genital odour [24].

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