Supplementary information for Figures:

1. References for Figure 1

Figure 1 Timeline figure showing the milestones in the history and development of FGF21

Since 2000, FGF21 has attracted great interest due to its pleiotropic effects in response to diverse physiological and pathological stress. With the knowledge of FGF21 expanding exponentially, our understanding of its biology is constantly undergoing modification, and the therapeutic value of FGF21 is being hotly discussed.

(1)2000 Identification as a novel FGF, FGF-21, preferentially expressed in the liver.

(2)2005 FGF21 is a novel metabolic regulator of glucose homeostasis and insulin sensitivity.

(3)2006 FGF21 delays the initiation of hepatocarcinogenesis

(4)2007 β-Klotho functions as a cofactor essential for FGF21 activity.

(5, 6)2007 FGF21 is a "missing link" in the biology of fasting

(7)2008 Serum FGF21 levels are increased in type 2 diabetes mellitus

(8)2008 Serum FGF21 levels are increased in obesity and are independently associated with metabolic syndrome.

(9)2008 Systemic administration of FGF21 corrects obesity in mice

(10)2009 FGF21 protects pancreatic acini in acute pancreatitis.

(11)2010 FGF21 targets the central nervous system to realize the metabolic benefits

(12, 13)2010 Hepatic and serum FGF21 levels are increased in NAFLD

(14)2011 The circadian rhythm of FGF21 in humans

(15)2011 Serum FGF21 levels are increased in human mitochondrial disorders

(16, 17)2012 FGF21 is a key mediator of the physiologic and pharmacologic actions of PPARγ in both adipose tissue and bone.

(18)2012 FGF21 extends lifespan in mice

(19, 20)2012 FGF21-mimetic antibody and analogue are developed for treating diabetes and obesity

(21, 22)2013 adiponectin is implicated in FGF21 actions

(23)2013 protects against cardiac damage.

(24, 25)2013 FGF21 defines an liver-neuroendocrine axis in response to nutritional challenge

(26, 27)2015 FGF21 requires neither UCP1 nor brite adipocytes to elicit weight loss and improve glucose homeostasis.

(28, 29)2016 FGF21 regulates sweet and alcohol preference

(30, 31)2016 Fibroblast activation protein cleaves and inactivates human FGF21

(32)2016 Defining nutritional and metabolic context of FGF21

(33)2018 FGF21 governs water consumption in response to ketogenic diet and alcohol

(34)2018 FGF21 protects against hypertension

(35)2019 Pegbelfermin, a PEGylated human fibroblast growth factor 21 (FGF21) analogue, alleviates non-alcoholic steatohepatitis in phase 2a trial

(36)2020 FGF21 has therapeutic value for prevention and treatment of pancreatitis.

(37)2021 FGF21 drives cell competition

(38, 39)2021 Nanoparticle drug delivery system is applied in FGF21 treatment

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