The link between cardiac disease and sleepless nights

Cardiac disease is often accompanied by a disruption of the physiologic sleep-wake cycle with a yet unknown mechanism. These disruptions of sleep-wake rhythmicity contribute considerably to the overall disease burden. The sleep-wake cycle is tightly controlled by the daytime-dependent diurnal secretion of melatonin whose secretion in turn is tightly controlled by sympathetic neurons which project from the superior cervical ganglia (SCG).

IP RIGHTS

PCT - Nationalization planned in EP/US 2023

Inflammation at the SCG as the underlying cause

The loss of diurnal rhythmicity in cardiac disease is accompanied by impaired pineal gland function and low melatonin levels. The SCG responds to cardiac disease with accumulation of inflammatory macrophages and the selective loss of pineal gland-innervating neurons.

REFERENCES:

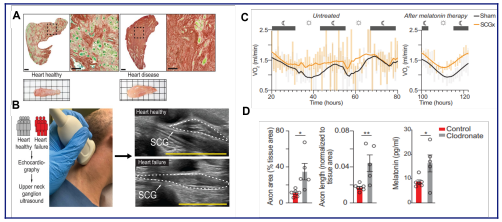
Ziegler et al., 2023, Science

01 Defective melatonin secretion warrants clinical investigation of melatonin administration for cardiac patients

02 Early anti-inflammatory intervention may prevent fibrotic scarring and ganglionic damage

03 SCG hypertrophy as biomarker for identifying patients most at risk for pineal denervation

04 Plans for a clinical study underway



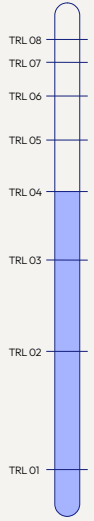
A) Significantly enlarged SCG in patients with heart disease B) Evaluation of human SCG morphometry by ultrasound in a prospective clinical study C) Assessment of diurnal rhythm in C3H/HeJ mice after sham and SCGx. SCGx resulted in a marked disruption of diurnal rhythm D) Local injection into the SCG ofmacrophage-inhibitor clodronate resulted in increased sympathetic axonal density within the pineal gland and melatonin levels.

CHALLENGE

One third of heart disease patients suffer from sleep problems and have low melatonin levels. Its synthesis occurs in the pineal gland and is, together with its secretion, controlled by sympathetic neurons that project from the SCG. The mechanism underlying the altered sleep-wake cycle in cardiac disease has remained elusive and there is no consensus as to the treatment. Interestingly, the SCG harbors heart-innervating neurons in addition to pineal gland-innervating neurons but its role has not been addressed yet.

INNOVATION

The data presented here revealed severe and likely irreversible immune-mediated destruction of sympathetic axons in pineal glands from humans and mice with cardiac disease . Spatial, single-cell, nuclear, and bulk RNA sequencing traced this defect back to the SCG, which responds to cardiac disease with accumulation of inflammatory macrophages, fibrosis, and selective loss of pineal gland–innervating neurons. Macrophage depletion in the SCG prevented disease-associated denervation of the pineal gland and restored physiological melatonin secretion identifying the mechanism by which diurnal rhythmicity in cardiac disease is disturbed and suggesting a target for therapeutic intervention.



01 Basic principles observed · **02** Technology concept formulated · **03** Experimental proof of concept · **04** Technology validated in lab · **05** Technology validated in relevant environment · **06** Technology demonstrated in relevant environment · **07** System prototype demonstrated in operational environment · **08** System complete and qualified

BayPAT

Innovation from Research & Science – BayPAT markets inventions on behalf of the Bavarian universities and universities of applied sciences.

An invention of **Technical University of Munich**

Technische Universität München

As one of the largest technology transfer offices in Germany, BayPAT evaluates and commercializes innovations from 28 research institutions. With our extensive experience and expertise in patenting and licensing technologies and our comprehensive range of services, we are your partner of choice. For more information visit www.baypat.de

Bayerische Patentallianz GmbH
Dr. Nicola Hoesch
nhoesch@baypat.de
+49 (0)89 5480177-29
Prinzregentenstr. 52
80538 München