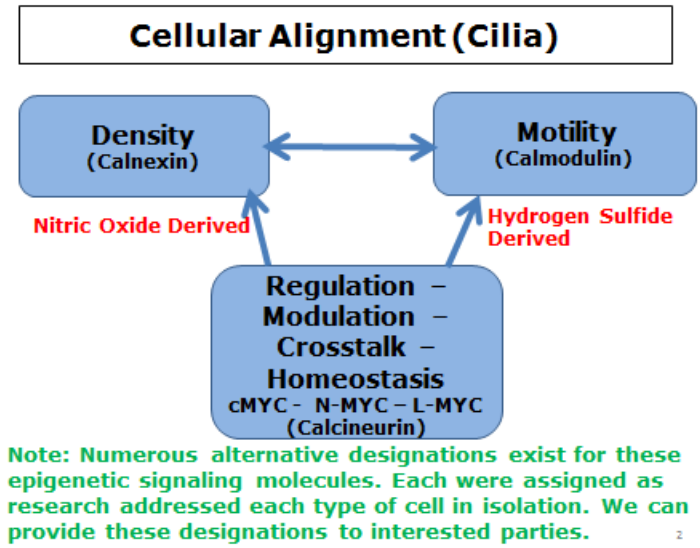
The following information starts with fibroblast growth factors and their impact on cardiac events.

The enzyme calcineurin is the epigenetic conversion to the trefoil of FGF19 - 21 - 23. Chirality factors are likely to be a primary cause for imbalances between calnexin and calmodulin that will impact arteries and ducts.



Cardiac research is using biomarkers as opposed to epigenetic markers. This same scenario is the primary pitfall for prevention of wearables to be truly effective tools for all of personalized medicine; not just for use by cardiologists; i.e. biomarkers are basically meaningless.

The document affixed to this article address biliary duct stenosis related to the epigenetic factors FGF19 - FGF-21 and FGF23.

For discussion purposes, the following link is also provided to discuss these epigenetic factors for obesity and adipose cell signaling.

http://diabetes.diabetesjournals.org/content/diabetes/early/2011/09/12/db11-0672.full.pdf

https://medicalxpress.com/news/2018-04-high-fgf-linked-recurrent-cardiac.html

High FGF-23 linked to recurrent cardiac events after ACS

April 23, 2018

(HealthDay)—Elevated fibroblast growth factor 23 (FGF-23) is associated with increased risk of recurrent major cardiovascular (CV) events in patients after an acute coronary syndrome (ACS), according to a study published online April 18 in *JAMA Cardiology*.

Brian A. Bergmark, M.D., from Brigham and Women's Hospital in Boston, and colleagues measured C-terminal FGF-23 in plasma samples for 4,947 patients within 30 days of ACS and with one additional CV risk factor in the Stabilization of Plaques Using Darapladib-Thrombolysis in Myocardial Infarction 52 trial.

The researchers found that FGF-23 concentration in the top quartile was independently linked to an increased risk of CV death or heart failure hospitalization and its individual components after multivariable adjustment for baseline clinical characteristics and established biomarkers (adjusted hazard ratio [HR], 2.35). There was also a correlation for increased FGF-23 concentration with an increased risk of all-cause mortality (adjusted HR, 2.27) and CV death, myocardial infarction, or stroke (adjusted HR, 1.42). The correlation between FGF-23 and CV risk, including CV deathor heart failure, was attenuated in women versus men ($P < 0.001$ for interaction).

"In patients stabilized after ACS, elevated FGF-23 concentrations may be associated with recurrent major CV events and all-cause mortality," the authors write.
Several authors disclosed financial ties to the pharmaceutical industry, including GlaxoSmithKline, which funded the study.

Explore further: **Lower hospital mortality for acute MI during heart meeting**
More information: **Abstract/Full Text**

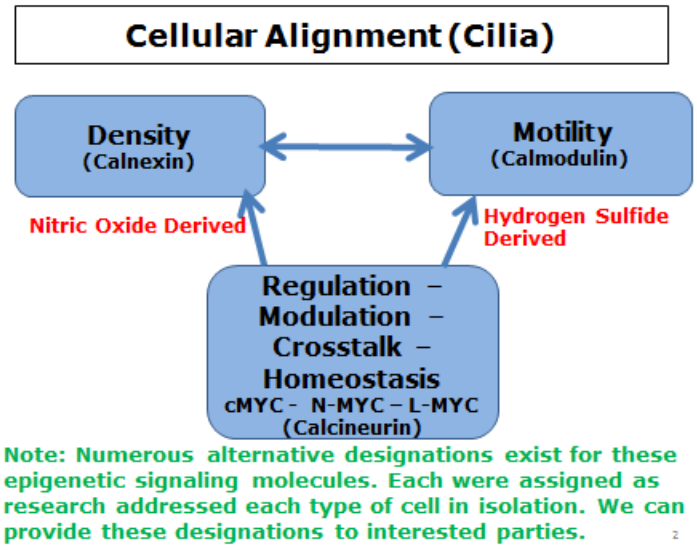
Journal reference: JAMA Cardiology

MCFIP - The following study links FGF19- 21 and 23 to biliary stenosis.

http://www.jbc.org/content/282/37/26687

Numerous other studies link FGF19, FGF21 and FGF23 individually as biomarkers for biliary stenosis.

Why? Our modeling of the epigenetic of these activities identified them as bioidentical to calcineurin; a master regulator for signaling of cilia. Refer to the following for discussion.



https://www.medpagetoday.com/meetingcoverage/easl/72354?xid=nl_mpt_DHE_2018-04-18&eun=g407160d0r&pos=6&utm_source=Sailthru&utm_medium=email&utm_campaign=Daily%20Headlines%202018-04-18&utm_term=Daily%20Headlines%20-%20Active%20User%20-%20180%20days

Biliary Fibrosis Stabilized with Obeticholic Acid

Biopsy study supports anti-fibrosis properties of agent

- by Ed Susman, Contributing Writer, MedPage TodayApril 15, 2018

PARIS -- A small biopsy study indicated that treatment with obeticholic acid may be able to stabilize and even reverse primary biliary cholangitis -- apparently confirming biomarker outcomes, researchers suggested here.

Six of 13 patients showed reversal of fibrosis by at least one stage; five patients showed that treatment with obeticholic acid stabilized their condition, and two had progressive disease, reported Christopher Bowlus, MD, of the University of California Davis medical campus in Sacramento.

In reporting the results of the POISE Trial substudy at the International Liver Conference, sponsored by the European Association for the Study of the Liver, Bowlus said, "These results are the first to provide histological evidence that long-term treatment with obeticholic acid may improve disease progression in primary biliary cholangitis."

He and colleagues observed that, in the four patients in the study who had baseline cirrhosis, fibrosis was reversed by at least one stage and three of these patients improved to a stage of fibrosis without cirrhosis.

"What is important here is that the majority of the patients in the study had either improvement in their fibrosis or no worsening after three years of treatment," Bowlus said.

The 13 patients in the study had been included in the parent POISE study; they had volunteered to undergo biopsy so the extent of progression or lack of it could be assessed. "These data are consistent with the previously reported anti-fibrotic effects with obeticholic acid therapy observed in pre-clinical models and in a placebo-controlled study in nonalcoholic steatohepatitis (NASH)," Bowlus said at a press conference.

He noted that primary biliary cholangitis is a chronic liver disease characterized by the inflammation and progressive destruction of bile ductules, cholestatis, eventual cirrhosis and death. "The diagnosis of the disease by using biomarkers makes the need for biopsy to prove the disorder an infrequent occurrence," he said.

Obeticholic acid is a potent, selective farnesoid X receptor agonist developed for the treatment of primary biliary cholangitis, Bowlus explained. The parent POISE trial enrolled 216 patients and showed that daily obeticholic acid

achieved greater improvements in alkaline phosphatase and bilirubin, indicators of liver function, after one year of treatment, he said.

To be eligible for the trial substudy, patients were required to have a baseline biopsy within a year from their first entry into the double-blind study. They then had to undergo another biopsy after treatment with obeticholic acid during an open-label extension of the study. There were 27 patients who had a baseline biopsy; 15 patients with paired biopsies and 13 patients for whom clinical data was adequate for analysis, Bowlus reported.

In the biopsy cohort, patients were about 58 years old; 12 of 13 were women; 85% were Caucasian; they had been diagnosed with primary biliary cholangitis for an average of 9.4 years. They were taking obeticholic acid for a mean of 3 years; and the mean time from initial to follow-up biopsy was 3.8 years. Nine patients had advanced fibrosis.

Five serious adverse events occurred in the trial, but that the investigators did not considered them likely related to treatment with obeticholic acid. One of those events was intra-abdominal hemorrhage related to the biopsy procedure, he said.

The effect of obeticholic acid on clinical outcomes in patients with primary biliary cholangitis is under evaluation in the COBALT post-marketing study, he said.

"This is an important observation," said press conference moderator Markus Cornberg, MD, of the Hannover Medical School in Germany. "However, these are small numbers, and there could be sampling bias in the way the study was conducted.

"Nevertheless," he told *MedPage Today*, "this drug does give us an option for use in patients who do not do well on other medications. We are glad we have an option. But in my view, I don't think this would be used on every patient."

Bowlus told *MedPage Today* that while the number of patients is small, the outcomes appeared to go in the right direction, "suggesting the finding is real."

Bowlus and Cornberg disclosed no relevant relationships with industry.