その他の臨床試験の現状

EPI-743

写真は発表時のみとさせて頂きます

小坂　仁　自治医科大学小児科

本邦での初症例が論文になりました

Kouga T, Takagi M, Miyauchi A, Shimbo H, Iai M, Yamashita S, Murayama K, Klein MB, Miller G, Goto T, Osaka H. Japanese Leigh syndrome case treated with EPI-743. Brain Dev. 2018 Feb;40(2):145-149

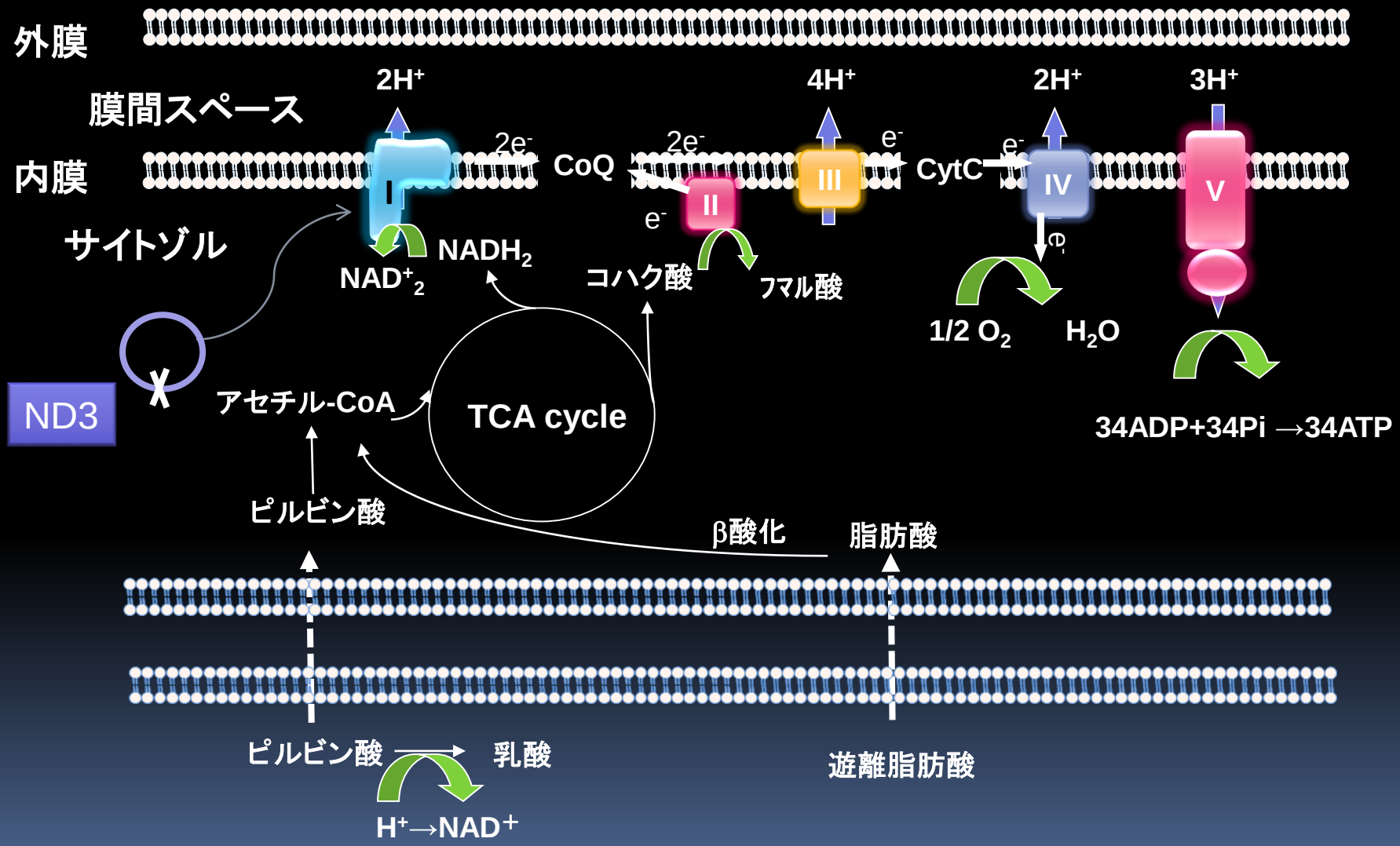
EPI-743; 本邦での初症例

主訴；発達遅滞・低緊張
妊娠分娩；異常なし、
7ヶ月時（写真）；頚定なく紹介
眼球運動少ないが、追視あり。唾液の嚥下は可能。
自発運動は少なく、僅かな四肢の動きのみ。

8ヶ月時; 自宅で呼吸停止。挿管され、気管切開目的転院軽度の開眼、自発運動はほとんどなし。

9ヶ月時; EPI-743投与開始。

電子伝達系の異常


外膜
膜間スペース
内膜
サイトゾル
2H+
4H+
2H+
3H+
2e-
CoQ
2e-
e-
CytC
e-
e-
I
II
III
IV
V
NAD+2
NADH2
コハク酸
フマル酸
1/2 O2
H2O
ND3
アセチル-CoA
TCA cycle
34ADP+34Pi →34ATP
ピルビン酸
β酸化
脂肪酸
ピルビン酸
乳酸
H+→NAD+
遊離脂肪酸

同様の遺伝子異常（ND3 m.10158T>C, p.S34P）報告例：5例

Pt1 died at　5 months of age after a rapid neurological deterioration.

Pt2　died at 7 months after a rapid neurological deterioration.

J Med Genet 2003;40:896–899

Pt3 died at age 3 years 9 months.

Pt4 died at 6 months.

Ann Neurol 2004;55:58–64

Patient died after an acidotic coma at age 9 mo.

Pediatr Res 55: 842–846, 2004

EPI-743開発者の来日

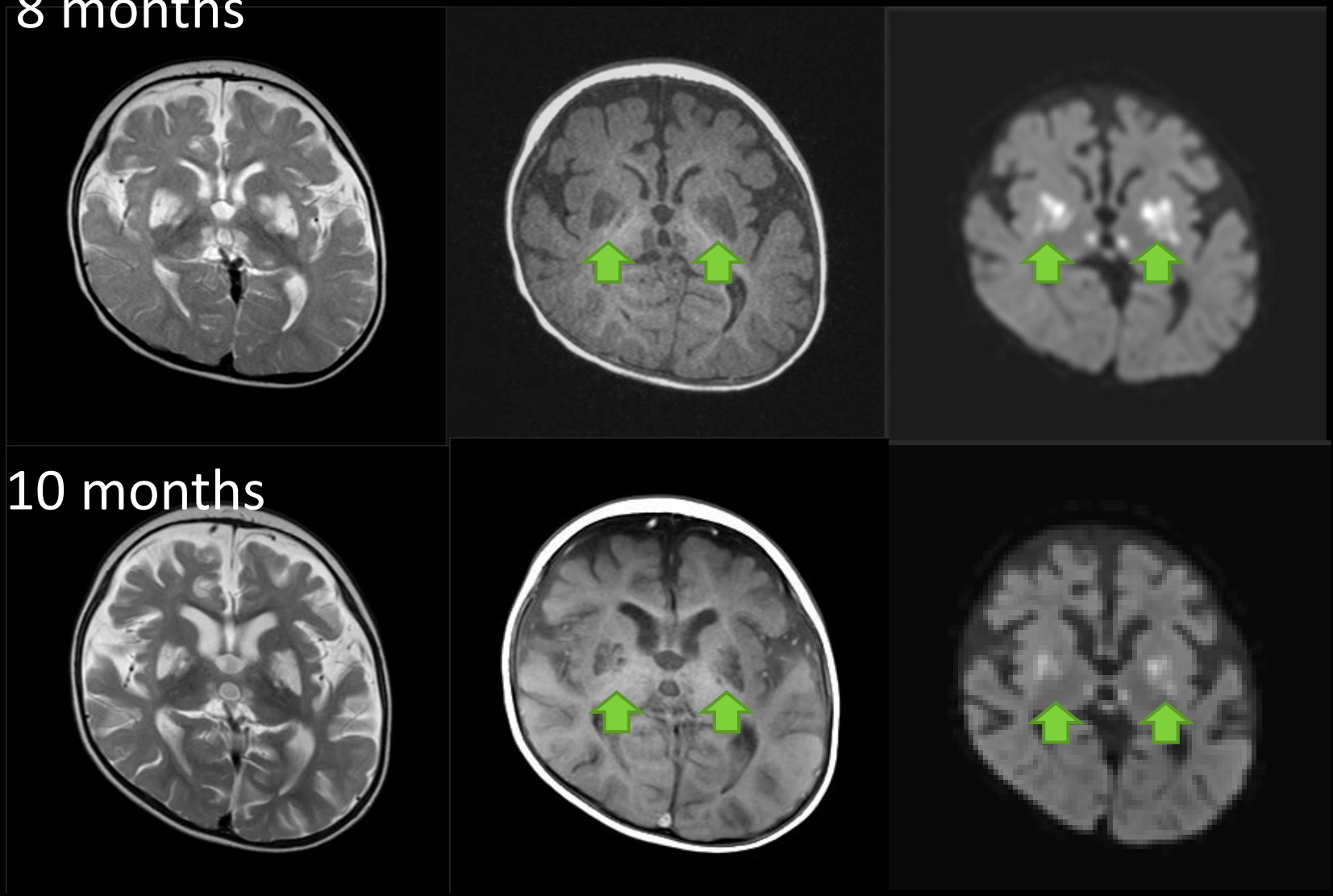
EPI もMillerと一緒に到着

EPI-743開始して二日後

自発運動・呼吸の出現
自力排便（2ヶ月ぶり）

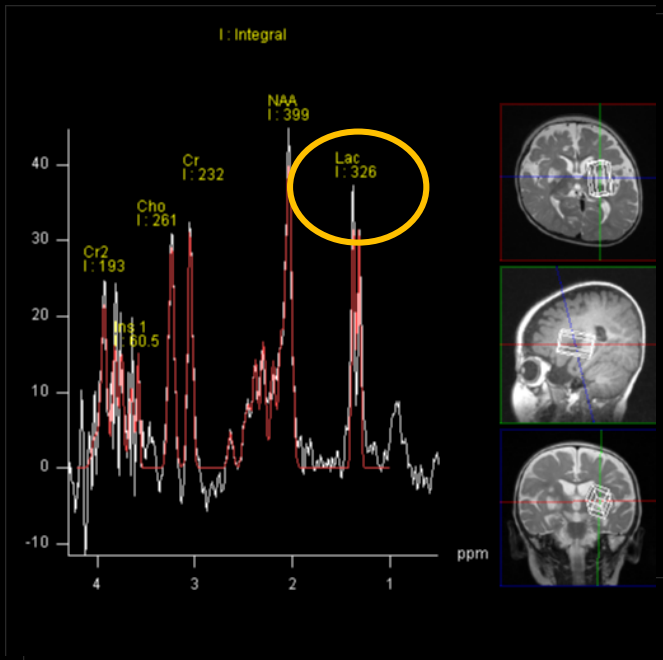
1W; 追視
手で吸引を嫌がる
表情が豊かになる

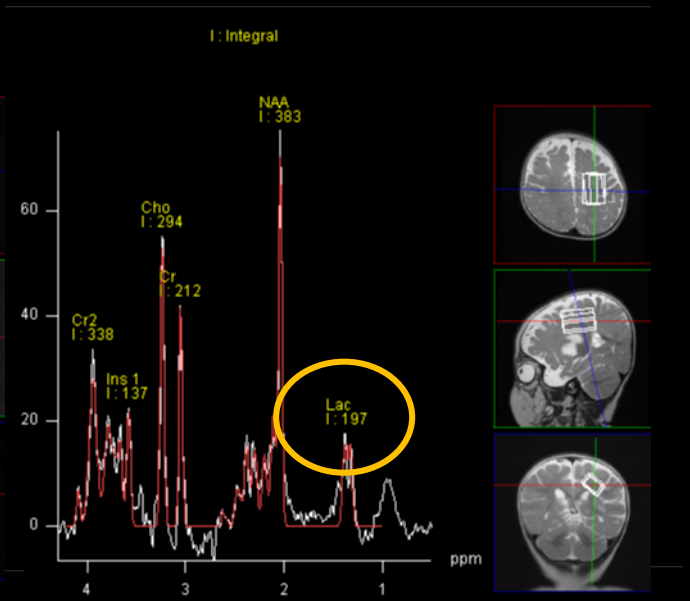
EPI開始後のMRI



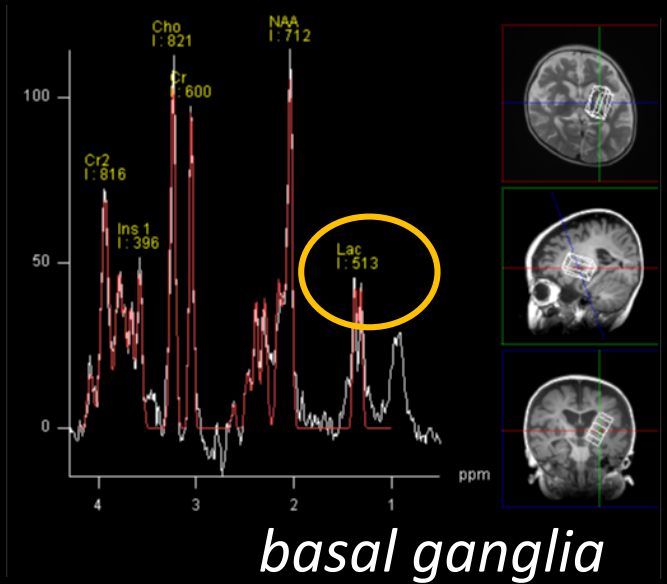
EPI開始後の乳酸値

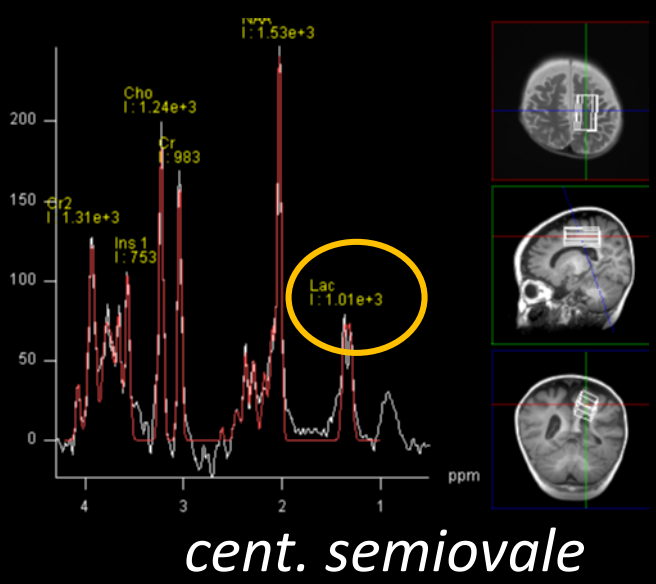
8mo





10mo





basal ganglia

cent. semiovale

11ヶ月; Miller さんへのクリスマスレター

もうすぐ小学校!

お返事1

Letter to the Editor

Is vatiquinone truly beneficial for Leigh syndrome?

“*Though promising, a single case is not sufficient for assessing the therapeutic effect of a so far un-approved drug. Drug effects need to be evaluated by a randomized, double-blind, placebo-controlled trial to prove or disprove a possible therapeutic effect.* 二重盲検をやらないと意味がない

“*How to exclude that the improvement was due to the natural course and not due to an effect of vatiquinone? There are several reports about improvement of the neurological deficits in mitochondrial disorders without treatment.*” 自然経過でもありうる

We have also experienced some gradual improvement in Leigh syndrome. However, we wanted to convey the fact that the patient exhibited rapid improvement of fine motor movement and bowel movements, and comparison with historical cases with the same mutation. 1例といえども事実を述べることは意味がある。

お返事2

We believe that you share the opinion that we really need more effective approved drugs for this devastating disease. Because Leigh syndrome is genetically very heterogeneous, it is very challenging to study in double-blind, placebo-controlled trials.

遺伝子のたくさんある病気で二重盲検というのは難しいけれど、この困難な病気に一緒に立ち向かいましょう