

chain deficiencies (Schuelke et al. 1999, de Lonlay-Debeney et al. 2000). Conversely, respiratory chain deficiency could be regarded as a secondary event in AGS, as cytokines are known to down-regulate mitochondrial gene expression with a reduction in cellular ATP levels (Lou et al. 1994, Lewis et al. 1996) and to mediate organ inflammation leading to mitochondrial dysfunction (Kaneda et al. 2003). Moreover, IFN- $\alpha$  has been shown to depress mitochondrial respiration in vitro, by depleting mitochondrial transcription factor A (Inagaki et al. 1997). However, none of the genes involved in cytokine pathways has been identified at the 3p23 locus.

Whatever the mechanisms of the oxidative phosphorylation defect, this observation should prompt the investigation of oxidative phosphorylation in AGS and conversely the assessment of CSF IFN- $\alpha$  in respiratory chain deficiency. We suggest, therefore, that genetic disorders of the mitochondrial respiratory chain should be regarded as a possible cause or consequence of AGS.

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#### References

- Azevedo-Martins AK, Lortz S, Lenzen S, Curi R, Eizirik DL, Tiedge M. (2003) Improvement of the mitochondrial antioxidant defense status prevents cytokine-induced nuclear factor-kappaB activation in insulin-producing cells. *Diabetes* **52**: 93–101.
- Crow Y. (2002) The genetics of Aicardi-Goutières syndrome. *Eur J Paediatr Neurol* **6** (Suppl A): A33–35; discussion A37–39, A77–86.
- Crow YJ, Black DN, Ali M, Bond J, Jackson AP, Lefson M, Michaud J, Roberts E, Stephenson JB, Woods CG, Lebon P (2003) Cree encephalitis is allelic with Aicardi-Goutières syndrome: implications for the pathogenesis of disorders of interferon alpha metabolism. *J Med Genet* **40**: 183–187.
- Crow YJ, Jackson AP, Roberts E, van Beusekom E, Barth P, Corry P, Ferrie CD, Hamel BC, Jayatunga R, Karbani G, Kalmanchay R, Kelemen A, King M, Kumar R, Livingstone J, Massey R, McWilliam R, Meager A, Rittey C, Stephenson JB, Tolmie JL, Verrrips A, Voit T, van Bokhoven H, Brunner HG, Woods CG. (2000) Aicardi-Goutières syndrome displays genetic heterogeneity with one locus (AGS1) on chromosome 3p21. *Am J Hum Genet* **67**: 213–221.
- de Lonlay-Debeney P, von Kleist-Retzow JC, Hertz-Pannier L, Peudrier S, Cormier-Daire V, Berquin P, Chretien D, Rotig A, Saudubray JM, Baraton J, Brunelle F, Rustin P, Van Der Knaap M, Munnich A. (2000) Cerebral white matter disease in children may be caused by mitochondrial respiratory chain deficiency. *J Pediatr* **136**: 209–214.
- Inagaki H, Matsushima Y, Ohshima M, Kitagawa Y. (1997) Interferons suppress mitochondrial gene transcription by depleting mitochondrial transcription factor A (mtTFA). *J Interferon Cytokine Res* **17**: 263–269.
- Kaneda M, Kashiwamura S, Ueda H, Sawada K, Sugihara A, Terada N, Kimura-Shimmyo A, Fukuda Y, Shimoyama T, Okamura H. (2003) Inflammatory liver steatosis caused by IL-12 and IL-18. *J Interferon Cytokine Res* **23**: 155–162.
- Kuijpers TW. (2002) Aicardi-Goutières syndrome: immunophenotyping in relation to interferon-alpha. *Eur J Paediatr Neurol* **6** (Suppl. A): A59–64; discussion A65–66, A77–86.
- Lebon P, Meritet JF, Krivine A, Rozenberg F. (2002) Interferon and Aicardi-Goutières syndrome. *Eur J Paediatr Neurol* **6** (Suppl. A): A47–53; discussion A55–58, A77–86.
- Lewis JA, Huq A, Najarro P. (1996) Inhibition of mitochondrial function by interferon. *J Biol Chem* **271**: 13184–13190.
- Lou J, Anderson SL, Xing L, Rubin BY. (1994) Suppression of mitochondrial mRNA levels and mitochondrial function in cells responding to the antiviral action of interferon. *J Interferon Res* **14**: 33–40.
- McEntagart M, Kamel H, Lebon P, King MD. (1998) Aicardi-Goutières syndrome: an expanding phenotype. *Neuropediatrics* **29**: 163–167.
- Rustin P, Chretien D, Bourgeron T, Gerard B, Rotig A, Saudubray JM, Munnich A. (1994) Biochemical and molecular investigations in respiratory chain deficiencies. *Clin Chim Acta* **228**: 35–51.
- Schuelke M, Smeitink J, Mariman E, Loeffen J, Plecko B, Trijbels F, Stockler-Ipsiroglu S, van den Heuvel L. (1999) Mutant NDUFV1 subunit of mitochondrial complex I causes leukodystrophy and myoclonic epilepsy. *Nat Genet* **21**: 260–261.
- Tolmie JL, Shillito P, Hughes-Benzie R, Stephenson JB. (1995) The Aicardi-Goutières syndrome (familial, early onset encephalopathy with calcifications of the basal ganglia and chronic cerebrospinal fluid lymphocytosis). *J Med Genet* **32**: 881–884.

#### List of abbreviations

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AGS	Aicardi-Goutières syndrome
ATP	Adenosine triphosphate
COX	Cytochrome c oxidase
CSF	Cerebrospinal fluid
GC	Gas chromatography
INF- $\alpha$	Interferon alpha
SCCR	Succinate cytochrome reductase

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## Erratum

### 'Balancing certainty and uncertainty in clinical medicine'

Hayward

DMCN Vol 48: 74–77

We would like to correct an error that was printed in the above mentioned article:

p 77: The sentence should have read: 'This article is based on Professor Hayward's inaugural lecture as Professor of Paediatric Neurosurgery, delivered at the Institute of Child Health...' and not 'This article is based on Professor Hayward's inaugural lecture as President of the Royal College of Paediatrics and Child Health at the Institute of Child Health...'

We sincerely apologize for this error.

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