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Comment: Mitochondria and carcinogenesis

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In a recent issue of this journal, C. Richter [1] published the hypothesis 'Do mitochondrial DNA fragments promote cancer and aging?'. According to Dr Richter's proposal, not only carcinogenesis, but also aging and other pathological or physiological conditions (such as development and evolution) may arise from the inclusion of mitochondrial DNA fragments in the nuclear genome.

This is a fascinating but not entirely new hypothesis. In a Comment published in this journal [2], H.I. Hadler claims priority owing to his numerous papers, published during the 1970s, demonstrating that many carcinogen metabolites and, in some instances, the carcinogen itself interfere with mitochondrial oxidative phosphorylation. According to Hadler "... when mitochondria were damaged, genetic material could be released from the mitochondria. The released material could behave like an oncogenic virus and enter the nuclear genome.".

It seems appropriate to recall that, already in the 1960s, our group demonstrated that physiological compounds, with carcinogenic activity, interfere with the mitochondrial process of oxidative phosphorylation. In particular, we showed that an *O*-aminophenol, 3-hydroxyanthranilic acid, inhibits the complex I of the respiratory chain and produces an uncoupling effect [3].

The importance of our work stems from the fact that 3-hydroxyanthranilic acid, a main intermediate in the physiological pathway of tryptophan metabolism, accumulates in some pathological conditions, particularly in bladder cancer [4].

It was shown that 3-hydroxyanthranilic acid and 3-hydroxykynurenine can induce experimental cancer of the bladder. Other synthetic *O*-aminophenols with cancerogenic activity were also found to inhibit oxidative phosphorylation [5].

Thus, this work was the first evidence of an experimental confluence between carcinogenicity and mitochondrial functions.

The importance of a hypothesis can be judged only when it receives adequate experimental support. Further work may provide more direct and convincing evidence on the role played by mitochondrial activity and/or by mitochondrial genetic material in carcinogenesis and other pathological conditions, including aging.

REFERENCES

[1] Richter, C. (1988) FEBS Lett. 241, 1-5.
[2] Hadler, H.I. (1989) FEBS Lett. 256, 230-231.
[3] Quagliariello, E., Papa, S., Saccone, C. and Alifano, A. (1964) Biochem. J. 91, 137-146.
[4] Alifano, A., Papa, S., Tancredi, F., Elicio, M.A. and Quagliariello, E. (1964) Br. J. Cancer 18, 386-389.
[5] Gorrod, J.W., Alifano, A., Papa, S. and Quagliariello, E. (1967) Cancer Res. 27, 668-673.

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