

## A quick look at the 2021's BASF publication on SDHI (PMID 33636213)

By Paule Bénit and Pierre Rustin



Paule Bénit

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In this publication by employees of BASF (seller of SDHI), it is (involuntarily) reaffirmed what we have been saying for 4 years: rodents are poor models to study the impact of a blockage of succinate dehydrogenase (SDH). One of our reasons is because they do not develop the tumors seen in humans with SDH deficiency and fail to reproduce the disease when inactivating SDH. These mice however develop other types of tumors in various organs when treated with SDHI. Here, contrary to numerous independent studies for 70 years (see for example Busch H & Potter VR 1952 J Biol Chem 198: 71-77) the authors conclude that blockade of SDH does not lead to accumulation of succinate... The second part reports the conclusion of an in-silico study that pretends to extend to human this prediction on the consequences of SDH blockade (no succinate accumulation). Again, such a conclusion appears in total contradiction with the observations (in different laboratories and by various technique - NMR in vivo, HPLC, biochemical quantification) made for many years establishing without possible dispute the accumulation of succinate (up to 4 times in fibroblast from Leigh patients and more than 100 times in paragangliomas) in the event of a SDH impairment or blockade (possibly associated with an abnormality of the lactate / pyruvate ratio). This accumulation of succinate is so constant that it is used as a mean of detecting SDH-deficient tumors in humans (eg Lussey-Lepoutre et al 2020 Eur J Nucl Med Mol Imaging 47: 1510-1517). On the whole this publication emphasizes the danger to use non validated, artificially build on purpose, in silico studies, easily misleading, to reach an overly desired conclusion: SDHI have no impact and their distribution should not be discontinued despite scientific evidences for their danger. It should also be stressed that SDHI toxicity at least in cultured human fibroblasts is mainly due to an oxidative stress resulting from SDH over reduction brought about by SDHI (Benit et al 2019 PlosOne 14). Such a role for oxidative stress associated with SDHI toxicity has been reported in a number of studies on fishes, batrachians, algae, etc. This voluntarily misleading BASF study leads to a strange, hazardous conclusion. It contradicts numerous previous and ignored scientific references. It is more deeply examined and discussed in our web site [EndSDHI.com](http://EndSDHI.com).