



Huge Modification of the Cell Theory by the Recent Discovery

of the Widespread Cell-derived Extracellular Vesicles

Irène Tatischeff 1,*

- ¹ Honorary CNRS and UPMC Research Director, Founder of RevInterCell, a Scientific Consulting Service, 91400, Orsay, France.
- * Correspondence: irene.tatischeff@eupmc.fr
- + Presented at the title, place, and date.

Abstract: The aim of this work is to discuss the necesity to strongly modify the powerful well-acknowledged cell theory 9 by taking into account the recently discovered universal cell-derivered extracellular vesicles (EVs). In a great breakthrough, EVs 10 are now known to mediate important cell's interconnections, which are resting on many still unknown mechanisms. There is a 11 missing step between the accumulated biological knowledge about EVs during two decades and the many recent preclinical 12 searches, dealing with a few human patients compared to controls, for EVs applications in oncology. In this case, the huge amount 13 of different cells-derived EVs generates an inextricable complexity. To evidence unknown EV-mediated mechanisms, a simple 14 cell model would be much more convenient. The microorganism Dictyostelium discoideum (Dd) is ideal to achieve this goal as a 15 wonderful eukaryotic in vitro and in vivo cell model. In 1998, we have discovered Dd EVs as mediating a new multidrug 16 resistance mechanism, and also the normal and physiological Dd cells-release of different EVs during the well-separated growth 17 and starvation-induced differentiation. Moreover, Dd cells are devoted with many other assets. Axenic Dd cells are very well 18

> suited for conditioned-medium experiments to study the influence of specifically generated Dd 19 EVs upon naive Dd cells, as will be shown in this presentation. 20

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