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Controversies and concept changes in erythrocyte aging studies: A Look into the dynamics of the research area

(1) Introduction

It is well known that mammalian erythrocytes are peculiar enucleated blood cells specialized for the oxygen transport within the organism. The finding of a definite life span for the circulating human erythrocytes (which in health and under normal condition has duration of approximately 120 days) dates from the early twentieth century. The accepted understanding of the removal of these cells from the bloodstream as the result of an aging process was not straightforward [1] and, presently, the mechanism by which the cell becomes senescent and at the edge of removal by the macrophages of the reticulo-endothelial system remains controversial.[2]

Present paper reports on work in progress regarding a research project on the dynamics of science within the life sciences and biomedicine taking the erythrocyte aging research as a case study. The paper focuses on the scientific debates and concept changes that follow the study of this biological / biomedical problem. It begins with a short description of the approach. Then, a brief overview of knowledge evolution as well as an account of major controversies embodied in the scientific literature is presented. Finally, these controversies are discussed in view of their role in knowledge generation and in the dynamics of the research area.

(2) The approach

Our project aims at exploring the dynamics of research on erythrocyte aging, its genealogy and changing pattern. In addition, it aims at analysing the meaning of controversies and concept changes in that dynamics. The basic idea was that identifying controversial issues would provide privileged insight into the dynamics of the research area. On that purpose, the paper draws on the (textual and rhetorical) analysis of published specialised papers.[3]

The analysis was directed towards the construction of a (provisional) timeline of major scientific achievements, as well as key experimental practices, whose value is at this phase mainly heuristic.

(3) A brief overview of knowledge evolution

Let us start in 1919 with the determination by Ashby of the length of life of transfused of human erythrocytes. This was an initial (reliable) determination of erythrocyte lifespan. The finding of the selective removal of old cells from the bloodstream is linked to the determination of cell lifespan using isotopic labelling some years later. Shemin and Rittenberg published that work in 1946. The assessment of cells of different age was made easy by the results of Borun and co-workers (1957) showing a correlation between age and cell specific gravity, which opened the possibility to use density fractionation to obtain cells of different age. From the mid-twentieth century onwards, much experimental work has been done,[4] aiming at the identification of the nature of the marker (or markers) of aging — which turned out to be a specific entity in the cell surface that would be responsible for the removal of old cells from the circulation — and of the mechanisms leading to such entities. Mostly, those studies

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[1] For an extensive review on that question see Clark (1988).

[2] Cf. Bosman *et al.* (2005) and Lang *et al.* (2005).

[3] It is also based on a previous experience of laboratory work on this theme.

[4] For reviews see Clark (1988) and Bartosz (1991).

were based on that procedure. Cell fractionation by density was, itself, object of controversy. Current studies use the loss of membrane phospholipid asymmetry (with phosphatidylserine externalization) as a tool to assess different kinds of cells. Lately, by the turn of the century, we can observe the emergence of a new understanding of the erythrocyte aging process mobilising apoptosis researchers and integrating the idea of a singular apoptosis process.

The analysis led to a selection of review papers marking distinct stages of knowledge. The reviews of Rous (1923) and Clark (1988) are enlightening of the early times. In the late 1990s, when the number of publications on "erythrocyte aging" dropped a lot, we should note the review by Bratosin and co-workers stating that "the search is not over and much work remains". It has been so with the work of that group on the apoptosis idea. The review by Lang and collaborators (2005) is a mark of these recent times. Also the one by Bosman and co-workers (2005), where the claim that "the processes leading to removal of erythrocytes from circulation are those of an execution phase of a apoptosis program" is pictured as conclusion that "may accelerate the slowly progressing research on erythrocyte aging".

(4) Some controversies and concept changes

Summing up, examples of major discussions among researchers have been, firstly, the proposal of the selective removal of the oldest circulating erythrocytes versus random destruction, then the different attempts to identify markers of aging as well as to establish the mechanisms leading to such entities, also the adequacy of density fractionation as a means to separate cells of different ages, and more recently description of this aging phenomenon as a kind of apoptosis / programmed cell death event in opposition to the idea of accumulation of injuries throughout the life span.

(5) Discussion and concluding remarks

The question now is how does this matter in view of a study focusing the dynamics of the research area? With this regard, we must stress the relationship between controversies, the observed concept changes and material practices. What has been the relevance of a different way of assessing distinct cells?

Present study is taken as a reference basis for a more detailed exploration that we are attempting to perform including the complementary approach of scientometric analysis.

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