

## Accepted Manuscript

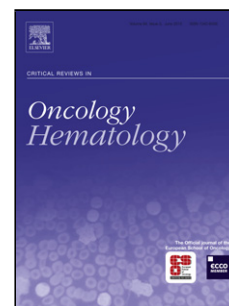
Title: The identification and isolation of CTCs: a Biological Rubik's Cube

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PII: S1040-8428(17)30420-1  
DOI: <https://doi.org/10.1016/j.critrevonc.2018.03.027>  
Reference: ONCH 2541

To appear in: *Critical Reviews in Oncology/Hematology*

Received date: 7-9-2017  
Revised date: 22-2-2018  
Accepted date: 29-3-2018



Please cite this article as: Mansilla C, Soria E, Ramírez N, The identification and isolation of CTCs: a Biological Rubik's Cube, *Critical Reviews in Oncology / Hematology* (2010), <https://doi.org/10.1016/j.critrevonc.2018.03.027>

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**The identification and isolation of CTCs: a Biological Rubik's Cube**

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**Abstract**

Liquid biopsy represents an alternative to conventional biopsies for the evaluation of tumors mainly due to its easy sampling. One of the main applications is the enumeration of Circulating Tumor Cells (CTCs) to evaluate tumor progression or response to treatment. The analysis of the functional characteristics of CTCs could give us much more information about their role in order to establish a more personalized treatment for the patients. The major issue that has to be solved is the isolation of the CTC population. Multiple protocols have been developed, however none of them has demonstrated to be the definitive one. In fact, a combination of these techniques has often been performed in order to obtain a purer and viable population of CTCs. In this review we have summarized for the first time the different combinatorial approaches used in the last years to optimize the isolation of CTCs and their limitations.

**Key words**

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