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Editorial

Striking Circulating Tumour Cells during Sleep

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Circulating tumour cells (CTCs) with stem cell-like properties and epithelial-mesenchymal transition phenotype are precursor cells responsible for dissemination and metastatic spread of cancer [1]. The prognostic importance of CTC detection and enumeration in several types of cancers is becoming more recognised [2]. For instance, an increase in CTC count is associated with cancer progression (and shorter overall survival) compared with a decrease in CTC count. In "cancer-free" subjects, the presence of CTC might indicate an early risk of cancer development [3]. However, CTCs are rare and present in very low concentrations in the blood circulation either as single cells (estimated as one CTC per 10^7 white blood cells per mL of blood) or as aggregates (circulating tumour emboli) that also show pronounced stemness features and metastatic potential [1]. CTC rarity, together with the current lack of reliable biomarkers that efficiently distinguish CTCs from other blood-borne cells, poses a major challenge for systematic and sensitive CTC detection and purification. Notwithstanding, nanotechnology is increasingly contributing to improved methodology developments in CTC detection and isolation [1,4]. Some of the most promising approaches include nanoparticle systems (e.g., cell enrichment with magnetic nanoparticles coated with anti-epithelial cell adhesion molecule antibody), stimuli-sensitive nanostructured platforms (e.g., thermo-responsive silicon nanopillars and nanowires patterned with recognition ligands to mimic the natural extracellular matrix) and integrated microfluidic devices [1,4].

Now, Diamantopoulou and colleagues [5] provide new insights on CTC intravasation, which, from a translational perspective, could potentially open up new diagnostics as well as more robust therapeutic and theranostic approaches in oncology. They show, that in both patients with breast cancer and mouse models, CTC generation is restricted to the rest-phase (during sleep), but the rest-phase CTCs have a much greater metastatic tendency than that of active-phase CTCs [5]. This unexpected pattern of CTC generation dynamics and augmented metastatic ability is under the influence of circadian rhythm hormones. More studies are needed to confirm these observations across a wider range of solid tumours and further identify additional factors that might contribute to spontaneous CTC intravasation. Nevertheless, the discovery of accelerated metastatic spread of breast cancer during sleep provides a new rationale for time-controlled strategies in metastatic cancer diagnostics and treatment response follow-ups. Considering this, time-controlled re-deployment of CTC detection nanotechnologies could provide unprecedented opportunities for more efficient CTC interrogation and multi-modal profiling. This, in turn, might lead to the discovery of new biomarkers, methodology refinement (e.g., plasmonic assays), and development of personalised anti-CTC therapies and theranostics.

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References

1. Lin, D.; Shen, L.; Luo, M.; Zhang, K.; Li, J.; Yang, Q.; Zhu, F.; Zhou, D.; Zheng, S.; Chen, Y.; et al. Circulating tumour cells: Biology and clinical significance. *Signal Transduct. Target. Ther.* **2021**, *6*, 404. [CrossRef] [PubMed]
2. Masuda, T.; Hayashi, N.; Iguchi, T.; Ito, S.; Eguchi, H.; Mimori, K. Clinical and biological significance of circulating tumor cells in cancer. *Mol. Oncol.* **2016**, *10*, 408–417. [CrossRef] [PubMed]
3. Ilie, M.; Hofman, V.; Long-Mira, E.; Selva, E.; Vignaud, J.-M.; Padovani, B.; Mouroux, J.; Marquette, C.-H.; Hofman, P. "Sentinel" circulating tumor cells allow early diagnosis of lung cancer in patients with chronic obstructive pulmonary disease. *PLoS ONE* **2014**, *9*, e111597. [CrossRef] [PubMed]
4. Ming, Y.; Li, Y.; Xing, H.; Luo, M.; Li, Z.; Chen, J.; Mo, J.; Shi, S. Circulating tumor cells: From theory to nanotechnology-based detection. *Front. Pharmacol.* **2017**, *8*, 35. [CrossRef] [PubMed]
5. Diamantopoulou, Z.; Castro-Giner, F.; Schwab, F.D.; Foerster, C.; Saini, M.; Budinjas, S.; Strittmatter, K.; Krol, I.; Seifert, B.; Heinzelmann-Schwarz, V.; et al. The metastatic spread of breast cancer accelerates during sleep. *Nature* **2022**, *607*, 156–162. [CrossRef] [PubMed]