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Selective Disruption of E-Cadherin–E-Cadherin Interactions in Inflammatory Breast Cancer Using Cold Atmospheric Plasma

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Cold atmospheric plasma (CAP) generates reactive oxygen and nitrogen species (RONS) capable of selectively inducing oxidative modifications in biomolecules, offering a promising tool for non-thermal biomedical applications. Recent studies have highlighted CAP's potential to modulate cell adhesion, signaling, and apoptosis [1]. Inflammatory breast cancer (IBC) [2] is a highly aggressive malignancy that, unlike many other cancers, retains strong E-cadherin expression, supporting dense metastatic emboli formation. In IBC, β-catenin remains membrane-bound, and the β-catenin degradation complex remains functional, preventing the activation of Wnt signaling even if β-catenin is released.

Using computer simulations, this study investigates whether CAP-induced oxidative stress can destabilize E-cadherin–E-cadherin interactions to weaken emboli integrity without activating oncogenic pathways [3]. Specifically, molecular dynamics (MD) simulations are conducted using the crystal structure of E-cadherin EC1–EC2 domains (Figure 1), with oxidative modifications introduced at residues susceptible to oxidation to model the effects of plasma-derived reactive species.

Preliminary simulation results suggest that oxidation of the E-cadherin–E-cadherin complex may cause a reduction in the stability of their binding interface, thereby weakening cell–cell cohesion critical for emboli stability.

Upon emboli disintegration, detached IBC cells are expected to undergo anoikis due to loss of adhesion signals. Moreover, any β-catenin released would be rapidly degraded via the APC–Axin–GSK3β complex, minimizing the risk of Wnt-mediated tumor progression.

This approach proposes a novel plasma-based therapeutic strategy to selectively destabilize metastatic emboli while preserving biological safety. Further simulations and experimental validations are required to fully evaluate the clinical potential of this strategy.

References

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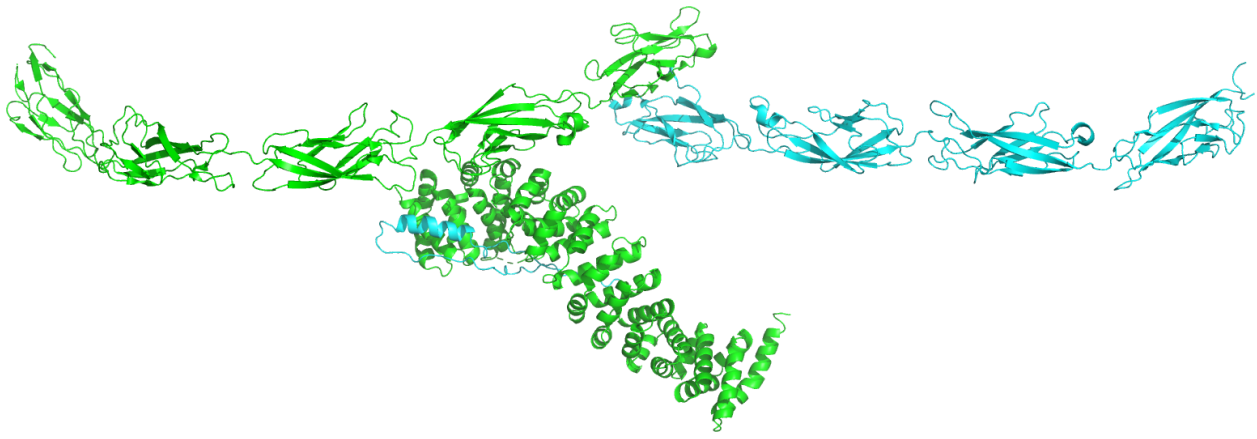

Figure 1. Ribbon representation of the E-cadherin–E-cadherin complex used in our MD simulations. Chain A is shown in cyan and Chain B in green. The structure illustrates the native adhesive interface prior to oxidative modifications induced by CAP.