



## Why the Hypocholesteremia must not be Neglected?

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During the last ten years studies on the role of cholesterol in the development and progression of cancer process and observations of severe hypocholesterolemia in patients with solid tumours and hematologic malignancies have been extended. The cancer cell incorporates cholesterol with avidity and reduces its serum level [1]. In normal cells, cholesterol binds sphingomyelin with very long-chained saturated fatty acids to form membrane lipid raft that acts as platform for proteins and receptors [2]. In the inner nuclear membrane lipid raft acts as platform for active chromatin anchoring and as resting place for transcription factors, vitamin D receptor and glucocorticoid drugs by regulating DNA duplication and RNA transcription [3-6]. Today, lipid rafts have been described as major platforms for signalling regulation in cancer [7]. Thus, cholesterol has a key role in cell physiopathology. When the blood cholesterol concentration in patient with initial tumour is normal or slightly increased, the effect of cholesterol in tumor growth is low [1], probably because normal lipid rafts house death receptor-mediated apoptotic signalling [7]. By modulating the apoptosis machinery of the cancer cell, it should be feasible to enforce its own cell death. Hypercholesterolemia facilitates the entry of cholesterol in the cells stimulating cell growth and inducing in time severe hypocholesterolemia [1]. It is possible that the high level of cholesterol in the cells increases the thickness of cell and nuclear lipid rafts by changing their function with two possible consequences; the apoptotic mechanism is blocked and cancer cells reduce their ability to suicide and/or lipid rafts include nucleic acids of cancer cells to form invadopodia responsible for metastatic diffusion [8]. Therefore the hypercholesterolemia influences the development of tumour and the severe hypocholesterolemia is a sign of tumour progression [1]. For this reason diet and obesity are now considered important risk factors for cancer development.

### References

1. Pugliese L, Bernardini I, Pacifico N, Peverini M, Damaskopoulou E, et al. (2010) Severe hypocholesterolaemia is often neglected in haematological malignancies. *Eur J Cancer* 46: 1735-1743.
2. Diaz-Rohrer B, Levental KR, Levental I (2014) Rafting through traffic: Membrane domains in cellular logistics. *Biochim Biophys Acta* 1838: 3003-3013.
3. Cascianelli G, Villani M, Tosti M, Marini F, Bartoccini E, et al. (2008) Lipid microdomains in cell nucleus. *Mol Biol Cell* 19: 5289-5295.
4. Albi E, Lazzarini A, Lazzarini R, Floridi A, Damaskopoulou E, et al. (2013) Nuclear Lipid Microdomain as Place of Interaction between Sphingomyelin and DNA during Liver Regeneration. *Int J Mol Sci* 14: 6529-6541.
5. Cataldi S, Codini M, Cascianelli G, Tringali S, Tringali AR, et al. (2014) Nuclear lipid microdomain as resting place of dexamethasone to impair cell proliferation. *Int J Mol Sci* 15: 19832-19846.
6. Bartoccini E, Marini F, Damaskopoulou E, Lazzarini R, Cataldi S, et al. (2011) Nuclear lipid microdomains regulate nuclear vitamin D3 uptake and influence embryonic hippocampal cell differentiation. *Mol Biol Cell* 22: 3022-3031.
7. Mollinedo F, Gajate C (2015) Lipid rafts as major platforms for signaling regulation in cancer. *Adv Biol Regul* 57: 130-146.
8. Weaver AM (2006) Invadopodia: specialized cell structures for cancer invasion. *Clin Exp Metastasis* 23: 97-105.