## Journal of Translational Science



Editorial ISSN: 2059-268X

## Relationship reconsideration between cancer, microorganisms, and platelets; focusing on possible mechanism of 'death triangle' as death cause

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The main cause of the in-hospital mortality and morbidity rate is not elucidated yet. Based on recent studies could be speculate that still cancer and infections are main cause of death. Human platelets are less named as death cause. The relationship between the so-called 'Death Triangle Machinery' (DTM) consisting of Cancer- Microorganisms-Platelets (CMP), either as indirect or direct cause(s), is not elucidated yet.

Nagaharu Tsukiji, *et al.* Blood 2018 postulated that human platelets (PLTs) participate in not only Thrombosis and Hemostasis but also other pathophysiological processes, including tumor metastasis and inflammation [1]. Though, the presumed role of PLTs in the development of solid organs has not yet been described completely [1-3].

Here is tried to draw attention to the DTM as a main cause of death, a mind provoking evidence-based attempt.

Microorganisms are small biologic antigens, which principally do not suppose to harm other organisms' health, but some kinds of microorganisms are extremely dangerous due to 1. their rapid proliferation and differentiation, 2. aggressiveness of their toxins, 3. capability of RNA/ DNA manipulation, 4. additive and/or synergistic collaboration with another microorganisms, and 5. Un-known mechanisms that limit respiration, blood circulation of their hosts.

There are three kinds of microorganisms that might harm patients' health and increase the rate of morbidity and mortality mainly 1. Bacteria 2. Viruses 3. Parasites. Bacteria are very small living entity that are made up of only one cell. Most types of bacteria aren't harmful, but some can infect vital organs and cause death. A few have even been linked with cancer. For instance, stomach cancer is one of the more common types of cancer worldwide. (3) Some of intercellular changes could lead to cancer over time, especially cancer in the lower part of the stomach. Although *H pylori* infection is assumed to be a major cause of stomach cancer, most people who have this infection not once developed stomach cancer. There are some evidences, which indicate people with *H pylori* might even have a lowered risk of some other types of cancer, although it is unclear exactly what role the bacteria play in these processes [3-5].

Apparently, none of known viruses could alone increase mortality and morbidity rate as well. Nevertheless, some of viruses in collaboration with each other increased risk of mortality and morbidity, either in an additive or synergistic manner. For example, chlamydia in combination with human papilloma virus (HPV) observed in cervix cancer. Furthermore, according to the World Cancer Report 2012-2014 data, 16% of cancers are caused by 'a combination' of viruses or bacteria infections: lymphomas can be triggered by the Epstein-Barr virus, which also causes mononucleosis [4].

Side effects of treatments are another kind of additive/synergistic relationship of the DTM association. Chemotherapy drugs with(out) antibiotics being used to cure cancer patients, while suppressing potential metastasis processes. Furthermore, the Guidelines indicate that testing for, and treating *H pylori* infection is recommended after removal of an early stomach cancer [4] subsequently patient become pancytopenic and develop chronic thrombocytopenia, which both pathological responses might activate death receptor (signaling) and increase mortality and morbidity rate, considerably [4,5].

Different studies postulated that in one hand, using antibiotics against *H pylori* infection aimed to eradicate it, which results in hematologic side effects i.e. (chronic) Immune Thrombocytopenia (ITP) in some patients [3,4]. Recall, chronic ITP could lead into sever bleeding disorders and even death, subsequently [5].

Isolated human platelets (PLTs) concentrates (PCs) produced in the blood banks center, which could be used to safe life of many patients suffering from bleeding disorders and meant to restore hemostasis especially cancer patients. (2) On the other hand, the lymphatic vessels express not only platelet-endothelial adhesion molecule-1(PECAM-1) but also the intercellular adhesion molecule-1 (ICAM-1) and vascular cell adhesion molecule-1 (VCAM-1) in the (un-)inflamed human small intestine and tongue, and lymphatic endothelium enhances VCAM-1 and ICAM-1 production with tumor necrosis factor-alpha [5,6]. Recall, adhesion molecules might increase risk of agglutination, aggregation of blood and lymphatic cells, (ir-)reversibly. How (non-)epithelial and/ or (non-) endothelial cells respond to abovementioned pathological overexpression is not elucidated yet.

How cancer-platelets-microorganisms (CPM) so-called 'death triangle' relate to each other? and how they affect (un-) known processes? is not elucidated yet. Which processes are either underestimated or overestimated is not clarified as well, completely.

What 'one' is observing about the CPM relationship is continuously changing concerning 1. the way of prognosis, 2. Diagnosis 3. Pretreatments and treatments, 4. cure and care plans. While none of the (non) standardized guidelines works; alternative new and mouthful.

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**Received:** November 09, 2018; **Accepted:** November 14, 2018; **Published:** November 16, 2018

J Transl Sci, 2018 doi: 10.15761/JTS.1000292 Volume 5: 1-2

Treatments also could not offer significant progressions (with all due respect) in lowering Mortality and Morbidity Rate of Diagnosed 5 years-Cancer Patient Survival Chance (MMRD5YCPSC). The MMRD5YCPSC phenomena still remains a mystery for Medici, after a Century, however. I hope that we as Medici together recognize, while no mistakes/side effects of treatments are allowed anymore, in 21th Century.

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J Transl Sci, 2018 doi: 10.15761/JTS.1000292 Volume 5: 2-2