Popular science abstract:

Cardiovascular diseases are the main cause of deaths worldwide. The direct cause in majority of cases is thrombosis – blockage of blood flow through blood vessels. To make prevention and medical treatment more effective it is crucial to identify new risk factors, both of environmental (external) and internal (localized inside human body) origin. Crucial players in thrombus (clot) formation are blood platelets, the smallest cells that can be found in human body. During normal, physiological response, platelets serve to efficiently seal any damage within blood vessels through formation of platelet plug that covers damaged area. Platelets can also form clots during pathological (non-physiological) situations in response to specific chemical signals, coupled with presence of toxins, ongoing inflammation or – more generally – during the course of many diseases.

Since 2004 it is known that other type of blood cells – neutrophils, fighting in the first line against invading pathogens – may form unusual, sophisticated structures from their own DNA, throwing outside cell to form „a net" to catch and kill invaders. That net (literally, the official term for this phenomenon is NET, acronym for Neutrophils Exteacellular Traps) is filled with many proteins with antibacterial, antiviral and antifungal properties. NET's-related DNA and proteins might activate blood platelets which in turn aggregate and form thrombi. Of importance, in many diseases associated with the elevated thrombotic risk (e.g. cancers, diabetes, asthma, reumatoid arthritis), concentration of NET in blood is elevated despite the lack of ongoing infections. Therefore, the idea was proposed to reduce thrombotic risk through pharmacological (through biologically active chemical compounds) blockage of NET formation. This strategy seems however risky, since radical „turning off" NET formation would likely weakens immune defense system to fight against pathogens.

To date, research in the topic of NET and platelet activation was focused on the effect exerted by a whole „lab-made NET" or different proteins, known to be present within NET, on platelets. In that context NET was considered as „accomplished" and rather static structure. Those studies, however important and – in many cases – groundbreaking, have not considered a possibly significant role of chemical reactions which are very likely to occur within NET and potentially change chemical nature of NET ingredients, making them even more prothrombotic. Research data suggests that reaction between hypochloric acid (HOCl, better known as main ingredient of house-hold bleach) – produced inside NET by MPO enzyme – and histones (main NET's protein, ~70%) might tip the balance. Specific chemical structure of histones and high affinity (measure of how much different compounds „like each other") of HOCl to histones make such reactions very likely. That would in turn generate a family of new, modified histones, never studied in context of platelet and neutrophils activation and thrombus formation.

Our preliminary experiments point that such processes are possible. The goal of proposed study is to complex investigate of how it is possible that NET may turn into the net of (thrombotic) risk and how to treat that? It is worth to notice that such approach – NET as dynamic chemical microenvorinment, with changing over time ability to affect blood cells – has never been raised before. Collecting such information would perspectivelly help to establish better and safer profilactic, diagnostic and healing of cardiovascular diseases.