With regard to cancer, however, the next question regarding HLA-G was obvious; it protects us during fetal life, but we still carry it inactive later on; therefore, does a growing tumor re-activate this gene system in order to grow while remaining undetected by our immunity?

The past few years have shown that many cancers do indeed have an active HLA-G. Studies also showed that the system produces 7 types of HLA-G proteins, 4 of which are membrane-bound (same as HLA-A or B or C), while 3 are soluble. They all do the same job: tell our immune surveillance that the cells producing these proteins are “OK” by suppression. So far, scientists have also identified at least 2 receptors for these proteins, the ILT-2 and ILT-4. Various tumors have been studied: melanoma, lymphoma (HD, NHL), acute leukemia, lung, SCLC, prostate, ovarian, bladder, colorectal and basal cell carcinoma. All have been shown to have an active HLA-G system, and the more active the gene is per tumor-cell population the more aggressive the tumor. What activates this system isn’t fully understood yet, but scientists have already determined that an active immune system is needed to make the tumor turn on the HLA-G. Tumor cells grown in vitro eventually did not turn on the HLA-G, because there was no threat against their survival in this safe microenvironment. Studies also have shown that Interleukin-10 (IL-10) and hypoxia are also factors that turn on HLA-G. To add to the complication of this subject, recently, two newer HLA systems, also playing a suppressor role, have been discovered: HLA-E and HLA-F. Studies are still under way to understand more about their roles; scientists know that HLA-E supports HLA-G and that they work together, but what are their triggers, and how important are they for normal or tumor cells?

While all these studies are trying to understand this complex new system, some scientists are already asking the next question: if we attack HLA-G or block its action or shut down its gene, can we “unmask” a tumor. If we can do this, there is a good possibility that our immune system will detect the tumor and clear it out naturally. Moreover, this approach can be applied to many cancers. Can this knowledge (that was in front of us this whole time) be the answer to punching cancer in the face?

Many are hopeful; however, we need to understand the details of HLA-G and its companions. For example, will shutting it down also block some other necessary normal function of theirs? Currently, research into therapeutics against this system is nearly absent. It is also noteworthy that even if everything goes right and we have a cure, it still leaves out many patients who are immune-compromised. These patients will never benefit from this “cure”.

To summarize, the discovery of the HLA-G,E and F systems has been like opening a Pandora’s box. We are now understanding that the same genetic system that helps us thrive during pregnancy, could also be hijacked by tumors later on to avoid getting detected by our “police” while continuing to grow. But will their exposure to immunity help us in reaching a natural way of killing many cancers with 1 method?? I can say that we are still toddlers learning to walk here. The Olympic medal for sprinting is still far away. However, not trying is not an option.

In conclusion, our curiosity and search for knowledge has never stopped us from discovering new facts around us, testing new theories of unsolved puzzles, and being hopeful for darker mysteries still out there. The question now is: Will this HLA-G vs. Tumors be such a discovery?

Our will and curiosity should have an answer soon!