PR - 025 - **Cooperation between T and B cells reinforce the establishment of bone metastases in a mouse model of breast cancer**

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Immune cells educated by the primary breast tumor and their secreted factors support the formation of bone pre-metastatic niche. Indeed, we showed that 4T1 tumor-specific RANKL$^+$ CD3$^+$ T cells, arrive at the bone marrow (BM) before metastatic cells and set the pre-metastatic niche. In the absence of RANKL expressed by T cells, there is no pre-metastatic osteolytic disease and bone metastases (BoMet) are completely blocked. Adding to the role of T cells, we have recently demonstrated that DCs assist RANKL$^+$ T cells activities at bone pre-metastatic niche, by differentiation into potent bone resorbing osteoclast-like cells, keeping their APC properties, providing a positive feedback loop to the osteolytic profile. Here we are showing that BM-derived CD19$^+$ B cells, from 4T1 tumor-bearing mice, also express RANKL. Analysis of trabecular bone mineral density by conventional histomorphometry and X-ray microtomography (micro-CT) demonstrated that RANKL$^+$ B cells cooperate with 4T1-primed CD3$^+$ T cells to induce bone loss. Moreover, RANKL expression by B cells depends on T cells activity, since experiments performed with B cells derived from 4T1 tumor-bearing nude BALB/c mice resulted in the maintenance of trabecular bone mass instead of bone loss. Altogether, we believe that 4T1-primed RANKL$^+$ B cells alone are not central mediators of bone loss *in vivo* but when associated with T cells induce a strong decrease in bone mass, accelerating both breast cancer progression and bone metastases establishment. Although several studies performed in different pathological settings, showed that B cells, positively and negatively impact on osteoclastogenesis, due to their capacity to secret pro or anti-osteoclastogenic cytokines, as far as we know, this is the first report showing the role of RANKL expression by B cells on breast cancer-derived bone metastases scenario.
Keywords: bone metastases;T cells;RANKL.

PR - 026 - **Immunomodulatory nanosystems with active targeting to phagocytes promote the production of neutralizing antibodies against the SARCoV2 virus in cows' colostrum**

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Biocompatible immunomodulatory nanosystems active targeted to phagocytes (NIBDAF) were developed by Embrapa based on green nanotechnology approach aiming to improve the efficacy of existing vaccines for cattle. Cows produce a significant amount of immunoglobulin in the colostrum and nutraceutical products with potential usage in viral disease prevention and control have become available for humans recently. The objective of our work was to develop a protocol for immunizing cows in order to produce hyperimmune colostrum with neutralizing activity against SARSCoV2.The recombinant RBD protein was obtained using the Expi293F™ expression system and purified by Ni-affinity chromatography. Pregnant cows were immunized with RBD-Alum adjuvant (InjectAlum®), RBD-NIBDAF or saline buffer (n=5 per group). The study was approved by the Ethics Committee on Animal Use (1915290721). Immunizations and serum sample collections were performed 45, 30, and 15 days before the expected birth date and on the day of parturition, along with colostrum. Production of IgG, IgG1, IgG2 anti-RBD, and viral neutralization were evaluated by ELISA in all samples. Cows immunized with recombinant RBD-Alum adjuvant produced higher amounts of all subclasses of antibodies compared to the RBD-NIBDAF group ($p<0.05$), except for IgG2. Moreover, no significant differences were observed in viral neutralization in serum samples between these two groups (32% in RBD-NIBDAF and 43% in RBD-Alum). In colostrum, NIBDAF provided 66% neutralization compared to 91% in the Alum group. These are promising results since RBD-NIBDAF without any other adjuvant have induced the production of neutralizing antibodies, especially the IgG2 subclasses known to be more effective in complement activation than other IgGs in bovine species. These results also support the use of cows as biofactories of neutralizing antibodies, providing an alternative for preventing future emerging and re-emerging diseases.
Keywords: Colostrum;bovine;nanosystems.