RJVS Research Journal of Veterinary Sciences

OPEN ACCESS

News & Comments

Modulation by All-Trans Retinoid Acid (ATRA)

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Dogs require the amino acid L-arginine (L-arg), which has also been linked to sustaining T-lymphocyte and natural killer (NK) cell function in people and mice. Arginase, which is produced by immunosuppressive myeloid cells such M2-type macrophages and myeloid-derived suppressor cells, metabolizes L-arg to L-ornithine and urea (MDSCs). In human investigations, it has been demonstrated that soluble mediators other than arginase, including IL-10, TGF-1, IL-6, and inducible nitric oxide synthase, are involved in tumour immune evasion (iNOS). TAMs and MDSCs have been demonstrated to develop into mature dendritic cells, macrophages, and granulocytes in both humans and mice when exposed to all-trans retinoic acid (ATRA), a vitamin-A derivative used to treat leukaemia and dermatological problems in people.

Dogs owned by clients and showing signs of cancer were given peripheral blood samples at Louisiana State University's school of veterinary medicine (LSU SVM). Following owners' informed agreement, a total of 15 mL was drawn from the jugular vein of dogs weighing more than 15 kg. To examine the effects of ATRA on cell viability, MDMs from two dogs were cultured with rhM-CSF and escalating doses of ATRA for five days.

The TME contains a variety of immunosuppressive myeloid cells as well as soluble mediators that aid in the development of tumours. The TME's alteration may strengthen anti-tumour immunity, making it an appealing treatment approach. Therefore, we sought to investigate ATRA's potential to modify canine MDMs in vitro. In MDMs subjected to non-cytotoxic dosages of ATRA, we noticed consistent 2-4-fold reductions in arginase, iNOS, IL-6, TGF-1, and CIITA mRNA transcripts. In comparison to vehicle controls, arginase activity was likewise consistently reduced in MDMs treated with ATRA. ATRA may be able to lower the immunomodulatory effects of canine macrophages, according to the findings of decreased pro-inflammatory (IL-6, iNOS) and immunosuppressive (arginase, TGF-1) mRNA transcripts and reduced arginase activity in MDMs treated with ATRA.

In the study, both the control and ATRA-treated samples of canine MDMs tested negative for MHCII. Previous publications have found that canine MDMs are either positive or almost negative for MHCII, with expression presumably depending on distinct study-specific circumstances for differentiation. MHCII expression was not increased by the ATRA treatment of canine MDMs in our investigation, but it did not also affect the expression of CD11b, CD14, or the costimulatory molecule, CD80. In the study described here, arginase activity in MDMs was reduced by ATRA, and arginase hindered the functions of canine T lymphocytes. ATRA may also be able to improve T-lymphocyte performance in microenvironments with high arginase activity because of the expression of arginase in macrophages.

In addition to demonstrating preliminary evidence that ATRA may be able to be used as a tool to adjust the immunosuppressive and proinflammatory capabilities of canine macrophages, the authors showed that arginase inhibited canine T-lymphocyte function. Without additional in vivo clinical investigations to assess the impact of ATRA on immunosuppressive myeloid cells within the complex TME of an immunocompetent canine host, it is impossible to judge the potential of ATRA as a canine cancer treatment.

Source: Veterinary Sciences

KEYWORDS

Canine, ATRA, myeloid cells, tumour associated macrophages, cancer, oncoimmunology, T-lymphocytes