Heparan sulfate-binding peptide as a potential inhibitor of tumor progression

Melo, C.M.[1, 2]; Pinhal, M.A.S. [1, 3]

[1]Universidade Federal de São Paulo, Dep. Bioquímica/Biologia Molecular
[2]Universidade of California San Diego, Dep. Pathology
[3] Faculdade de Medicina do ABC, Dep. Bioquímica

INTRODUÇÃO. Heparan sulfate (HS) is important in cell proliferation,migration and adhesion. **OBJETIVO:** Evaluate the effect of HS-binding-peptide in cancer. **MATERIAL E METODOS:** Tryptophan had emission measured with different heparin concentrations to verify peptide targeting in vitro. Zebrafish whole mount immunostaining were performed using anti-HS-antibody and peptide targeting in vivo analysis was performed injecting fluorescent peptide in zebrafish embryos Fli1:(eGFP). MDA-MB-231 migration was also tested by 'wound healing' and xCELLigence-real-time-cell-analysis transwell coated with matrigel. In vivo invasion was tested injecting MDA-MB-231-eGFP-brain-metastasis into chicken embryos. Viability/proliferation of MDA-MB-231was tested by xCELLigence coated with matrigel, AlamarBlue and BrdU. Also,3D-culture viability was analyzed using triple negative breast cancer cells derived from patient (patient-derived-xenograph, PDX). Angiogenesis in vivo, Fli1:(eGFP) were treated with HS-binding-peptide and sub-intestinal vessels were evaluated. E x vivo angiogenesis, mice aortas were plated and analyzed after treatment. In addition, in vitro capillary formation using RAEC cells was performed. Also, we analyzed the angiogenesis inhibition mechanism using in a xCELLigence transwell coated with collagen typeI using FGF-2orVEGF to analyze the HUVEC migration and proliferation. Peptide was tested in vivo using PDXc ells after transduction with lentivirus-red-fluorescent-protein. PDX cells labeled with red-fluorescent-protein were selected by puromycin and FACS. After selection, these cells were injected into Fli1:(eGFP) yolk sac and treated. **DISCUSSÃO E RESULTADOS**: The peptide interacts with heparin/HS in vitro, since heparin changed the emission of tryptophan. Also, the peptide was capable to bind in HS in vivo. Due to peptide was retained into yolk sac that presents higher HSamount.MDA-MB-231migration is decreased by peptide. However, we verified that invasion was not inhibited. It seems that in vitro migration inhibition was not sufficient to decrease in vivo invasion. Proliferation/viability of triple negative breast cancer cells were not affected by the treatment. In vivo,ex vivo and in vitro assays showed that peptide inhibits angiogenesis. xCELLigence analysis conclude that HUVEC proliferation byFGF-2 is affected by HS-binding-peptide. HS-binding-peptide decreased tumor progression in vivo and raised embryos survival. **CONCLUSAO:** We can conclude that peptide binds to HS in vitro and in vivo, affecting FGF-2proliferation and causing angiogenesis inhibition. This inhibition was sufficient to decrease tumor development and increase survival.

Keyword: cancer, heparan sulfate, therapy
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