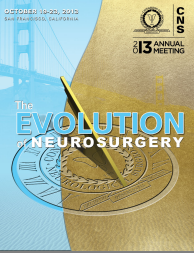


# Does BMP-2 Really Cause Cancer? A Systematic Review of the Literature.

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## Introduction

Recently, the use of recombinant human bone morphogenetic protein-2 (rhBMP-2) in spine surgery has been the topic of much debate as rhBMP-2 has been reported to be associated with a higher incidence of developing new malignancy (3.8% vs. 0.89% in control) (Carragee, Spine J 2011).

## Methods

A systematic review of the published literature was performed using the MEDLINE database. Only studies directly addressing BMP-2 and cancer were included. Articles were categorized by the study type (in vitro, animal, or human), primary malignancy, cancer attributes, and whether BMP-2 was pro-malignancy or not.

## Results

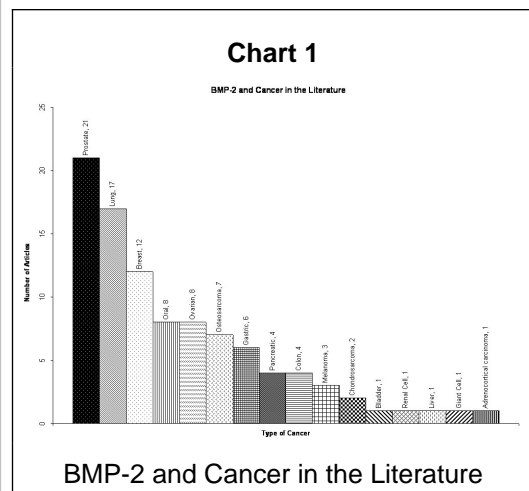
A total of 4466 articles were reviewed. Of those, 412 articles made reference to both BMP-2 and cancer, 93 of which were found to directly examine the role of BMP-2 in cancer. Forty-two studies were in vitro, 32 studies used human specimens, and 23 were animal studies. Forty-three studies concluded that BMP-2 enhanced tumor function, whereas 12 studies found that BMP-2 suppressed malignancy. Thirty-eight studies did not examine whether BMP-2 enhanced or suppressed tumor function. Eight in vitro studies demonstrated BMP-2 dose dependence (6 enhancement, 2 suppression), while 6 showed no dose dependence (4 enhancement, 2 suppression). One human study demonstrated BMP-2 dose dependence for tumor suppression and 2 studies showed no dose dependence for tumor enhancement. Five animal studies showed BMP-2 dose dependence (3 enhancement, 2 suppression) and 4 demonstrated no dose dependence (3 enhancement, 1 suppression). However, no study showed that BMP-2 causes cancer de novo.

## Learning Objectives

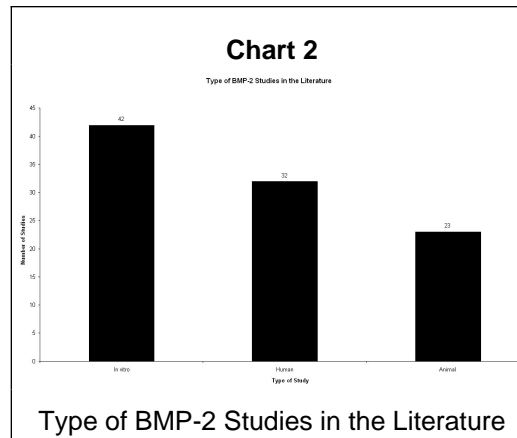
At the end of this session the audience should be able to: 1) better understand the complex pathways of BMP signaling, 2) realize the powerful role BMP plays in cell homeostasis, 3) develop an understanding of the complexity of BMP and its potential effects on cellular proliferation, 4) understand the current knowledge of BMP and its effects on malignancy.

## Conclusions

Currently, conflicting data exist with regard to the effect of exogenous BMP-2 on cancer. The majority of studies addressed the role of BMP-2 in prostate (21%), lung (17%), and breast (12%) cancers. Most were in vitro studies (43%) and examined the primary growth of malignancies (56%). Of 93 studies, there was no demonstration of BMP-2 causing cancer de novo. However, 46% of studies suggested BMP-2 enhances tumor function, motivating more definitive research on the topic that also includes clinically meaningful dose- and time-dependence.



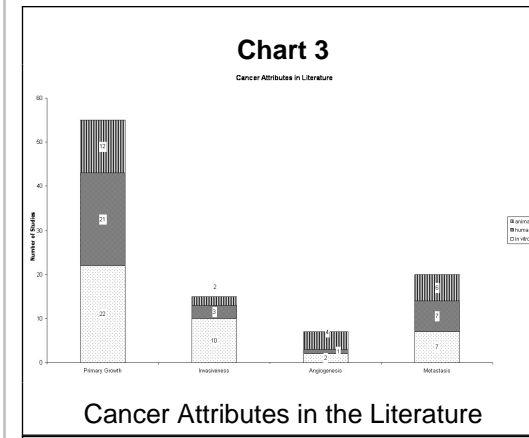
BMP-2 and Cancer in the Literature



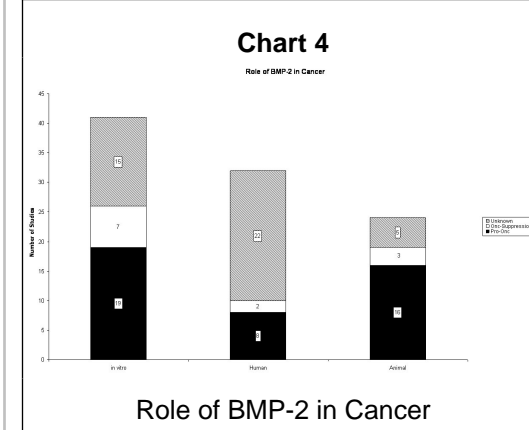
Type of BMP-2 Studies in the Literature

## References

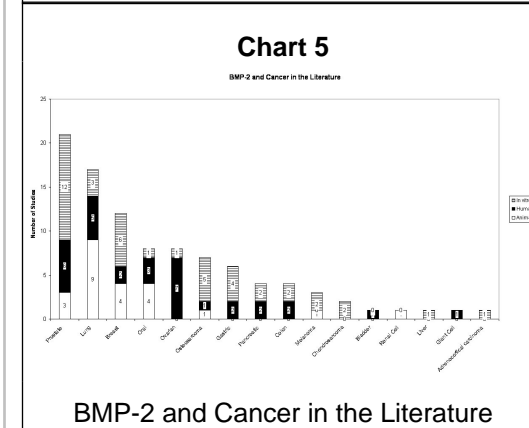
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Cancer Attributes in the Literature



Role of BMP-2 in Cancer



BMP-2 and Cancer in the Literature