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2011 Molecule of the Year

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With the potential to induce dormancy of prostate cancer stem-like cells in bone tissue, BMP7 has been named the 2011 Molecule of the Year.

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The International Society for Molecular and Cell Biology and Biotechnology Protocols and Research (ISMCCBBPR) has named bone morphogenetic protein 7 (BMP7) as the 2011 Molecule of the Year.

BMP7 is being recognized for its potential to induce dormancy in prostate cancer stem-like cells in bone microenvironments. This function of BMP7 was highlighted by Southern Illinois University School of Medicine researcher Kounosuke Watabe and colleagues in a paper published in the *Journal of Experimental Medicine* (1).

“Curing cancer is not a very simple thing; we’ve been trying for a long time without finding a cure. But we believe that this BMP7 is a key molecule that controls the dormancy and recurrency switch of cancer stem-like cells,” said Watabe. “My personal opinion is that if we can keep a tumor cell dormant forever, it’s almost as good as a cure.”

In their paper, Watabe and colleagues wanted to understand the factors in the microenvironment that controlled the dormancy and recurrence of prostate cancer stem cell growth in bone tissue. By co-culturing bone stromal cells with prostate cancer stem-like cells, the group found that cancer cell growth was suppressed.

“Cancer stem-like cells are still a hypothesis, they’re not a completely proven idea yet. But we believe that there are such cancer stem cells exist and make up about 1-2% of cancer cells,” said Watabe. According to this hypothesis, these cell can differentiate into other cells and are resistant to chemotherapy.

Through a series of follow-up experiments, the researchers discovered that BMP7, which was secreted by bone stromal cells, was responsible for this suppression of cancer stem-like cell growth. Specifically, Watabe’s team found that BMP7 induced senescence in these cancer cells by affecting several pathways that induce senescence in the cells, namely the p38, p21, and NDRG1 pathways.

All in all, BMP7 is not a new protein. Previous research has shown that it is involved with bone homeostasis and vertebrae development. Furthermore, the Federal Drug Administration has approved its use to aid bone repair during surgical procedures.



Crystal structure of bone morphogenetic protein 7 (BMP7), the 2011 Molecule of the Year, is depicted in complex with the secreted antagonist Noggin. Source: Wikipedia

After their in vivo experiments, Watabe and his team tested a treatment of BMP7 in a mouse model of bone cancer. They found that the continuous injection of BMP7 suppressed the growth of the tumor cells. But more importantly, when the researchers stopped treatment of BMP7 in the mouse models, the tumors grew back.

“Most of people believe that senescence is an irreversible cellular state. But when we stopped BMP7, the cells came back to grow. So, this is happening in cancer stem-like cells. This is a really conceptual breakthrough,” said Watabe.

Now, the next step is to see if this research can be translated to treat humans cancer patients to keep cancer stem-like cells dormant and prevent recurrence. The idea would be to develop a small drug molecule that mimics the function of BMP7 and trigger the same pathways in cancer stem-like cells.


Meanwhile, Watabe is also literally on the move. He’s just accepted a position at the University of Mississippi Cancer Institute, where he will be the associate director of basic research. So, as he’s unpacking boxes and figuring out the phone system, he’s also keeping an eye out for clinical collaborators. “This is a new environment with many excellent scientists, a nice move forward,” said Watabe.

References

1. Kobayashi, A., H. Okuda, F. Xing, P. R. Pandey, M. Watabe, S. Hirota, S. K. Pai, W. Liu, K. Fukuda, C. Chambers, A. Wilber, and K. Watabe. 2011. Bone morphogenetic protein 7 in dormancy and metastasis of prostate cancer stem-like cells in bone. *The Journal of Experimental Medicine* 208(13):2641-2655.


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