РОЛЬ SNAIL, SLUG AND TGB- ФАКТОРА ПРИ ОСТЕОСАРКОМЕ

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Резюме: Наиболее распространенной первичной злокачественной опухолью костей, поражающей детей и подростков, является остеосаркома. Пятилетняя выживаемость при регионарных опухолях обычно составляет от 60 до 70 процентов, но у пациентов с рецидивирующими или метастатическими опухолями она снижается до 20 процентов. Прогноз по-прежнему плохой даже при самом современном неоадъювантном лечении. Когда остеосаркома поражает легкие, это может быть фатально. Здесь регуляторная сеть Slug имеет важное значение для эпителиально-мезенхимального перехода и для прямого и непрямого распространения раковых клеток в критические органы

Ключевые слова: ЭМП - эпителиально-мезенхимальный переход, МЭП - мезенхимально-эпителиальный переход, SNAIL1 - цинковый палец семейства улиток

THE ROLE SNAIL, SLUG AND TGB FACTOR IN OSTEOSARCOMA

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Resume

Osteosarcoma is the most prevalent primary malignant bone tumor in children and teenagers. Patients who have recurring or metastatic tumors have a 5-year survival rate of only 20%, whereas the 5-year survival rate for regional tumors is normally between 60 and 70%. Despite the most advanced neoadjuvant treatment, the prognosis remains poor. It can be lethal when osteosarcoma spreads to the lung. In this case, the epithelial-mesenchymal transition and the direct and indirect spread of cancer cells to vital organs depend on the Slug regulatory network. In instance, slug and snail signaling pathways contribute to cancer invasion and metastasis.

This work aims to understand the role of Slug and Snail transcriptional factors in controlling EMT in osteosarcoma metastases.

Keywords:EMT- epithelial mesenchymal transition, MET mesenchymal–epithelial transition, SNAIL1- Snail family zinc finger 1

Introduction

Osteosarcoma

Osteosarcoma is an aggressive malignant disease that usually spreads to the patient's lungs after first affecting the arms and knee bones. It generates osteoid matrix, malignant fusiform cells, and aberrant bone growth. Abarrategiet al. (2016) state that patients who have disorders that impact their "DNA" development are more likely to develop "osteosarcoma." With the emergence of bone cancers, which are often brought on by DNA cell mutations that degrade the tissues, the incidence of "osteosarcoma" rises. A number of cancer types, including "osteosarcoma" bone cancer, usually cause lung damage, according to Lu et al. (2018).

From cancer cells that have already been impacted, the body's genetic differentiation can be seen.

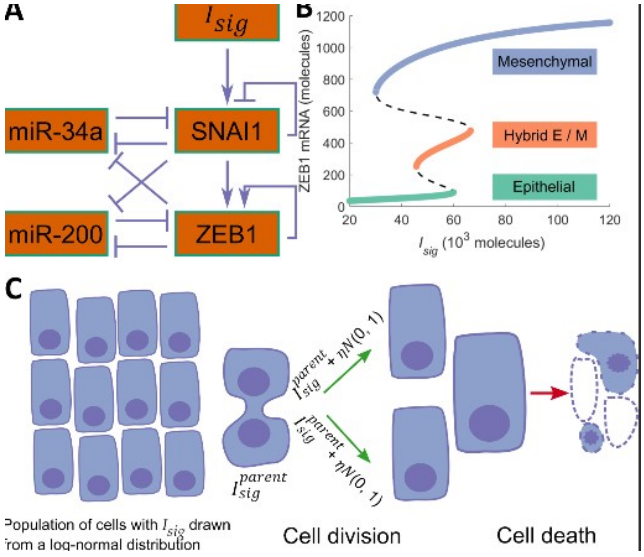
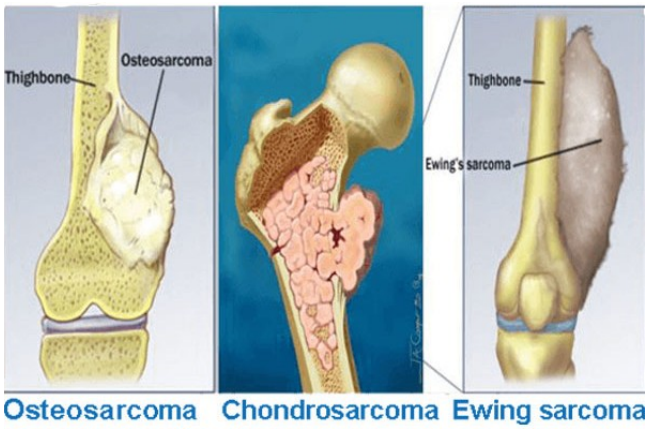


Figure 1.2: Cell Division

(Source: Azevedo *et al.* 2020)

The diagram above illustrates the many cell divisions, cell death, and the way cells change from one place of the body to another. Additionally, the cell division shows the likelihood that the "Cancerian" cells may change from one area to another. As a result, "osteosarcoma" or bone cells eventually develop into cancer cells, and the bunch cells frequently investigate the possibility of acquiring other body parts. Over time, the cells improve the cell division in the patients' lungs, increasing the likelihood that they will develop "lung cancer." The "epithelial" cells have trouble receiving the right treatment because of the genetic alterations that increase the likelihood of receiving a bad diagnosis. The presence of the disease can be explained by the fact that "osteosarcoma" in the human body denotes a swelling in the outer muscles of the joints. The presence of "osteosarcoma" is frequently indicated by pain in the joints and muscles.



Histopathology

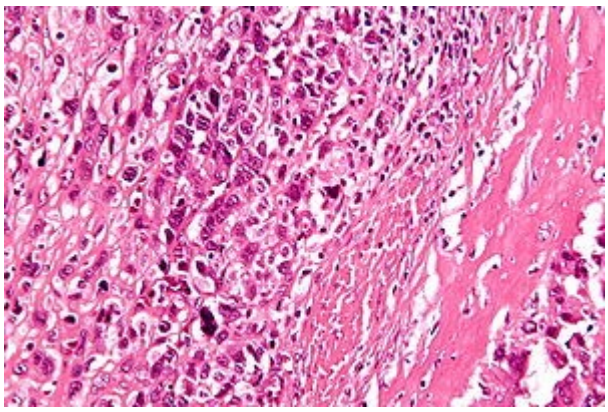


Figure 1.5: Skeletal osteosarcoma

(Source: Wadhwa, 2014)

A tumor composed of malignant cells that produce osteoid is called skeletal osteosarcoma. A chondroid and fibromatoid ground material is common in many tumors. However, all are highly malignant, and over 80% of them die as a result of metastasis. A roentgenogram offers vital proof for an accurate diagnosis for each of them (Wadhwa, 2014).

Zinc-finger E-box-binding, SNAIL, and basic helix–loop–helix transcription factors are among the transcription factor proteins that are implicated in this shift in cell differentiation and behavior, according to Lamouille et al. (2014). Their functions are precisely regulated at the post-translational, translational, and transcriptional levels.

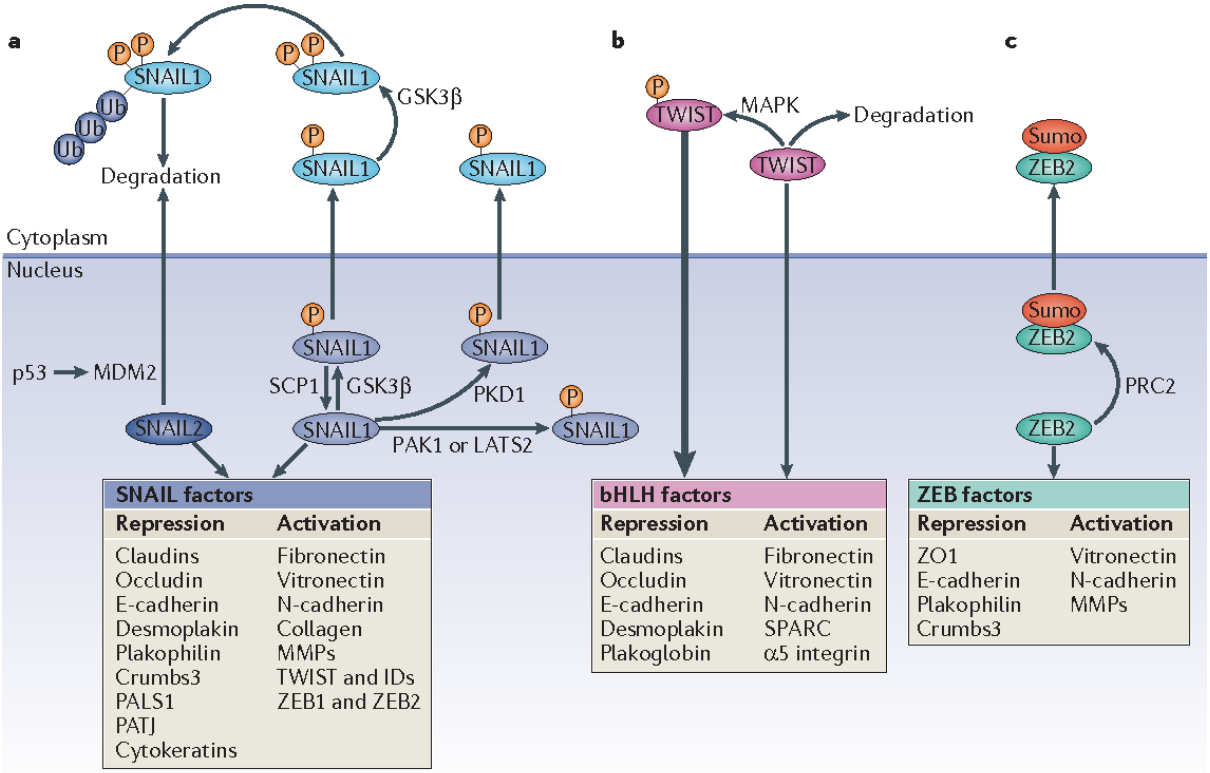


Figure 2 | **Roles and regulation of major EMT transcription factors.** Epithelial–mesenchymal transition (EMT) is driven by

Materials and Methods

The involvement of the snail, slug, and (twist1, twist2, zeb1, zeb2, E-cadherin, TGF-B3, vimentin) in the epithelial-mesenchyme transition in lung metastasis in osteosarcoma has been analyzed in this work by secondary research. According to Johnston (2017), secondary research makes the study more economical and efficient by assisting in the collection of pertinent data on the established fact. Using keywords like "epigenetic control," "cadherin expression," "EMT metastasis matrix," and "embryonic development in osteosarcoma," articles pertaining to "EMT metastasis" are simultaneously searched on the "Pubmed.com website" to gather information about the "underlying epigenetic controls," "E-cadherin expression," "N-cadherin expression," and "anoikis resistance" within the "EMT metastasis."

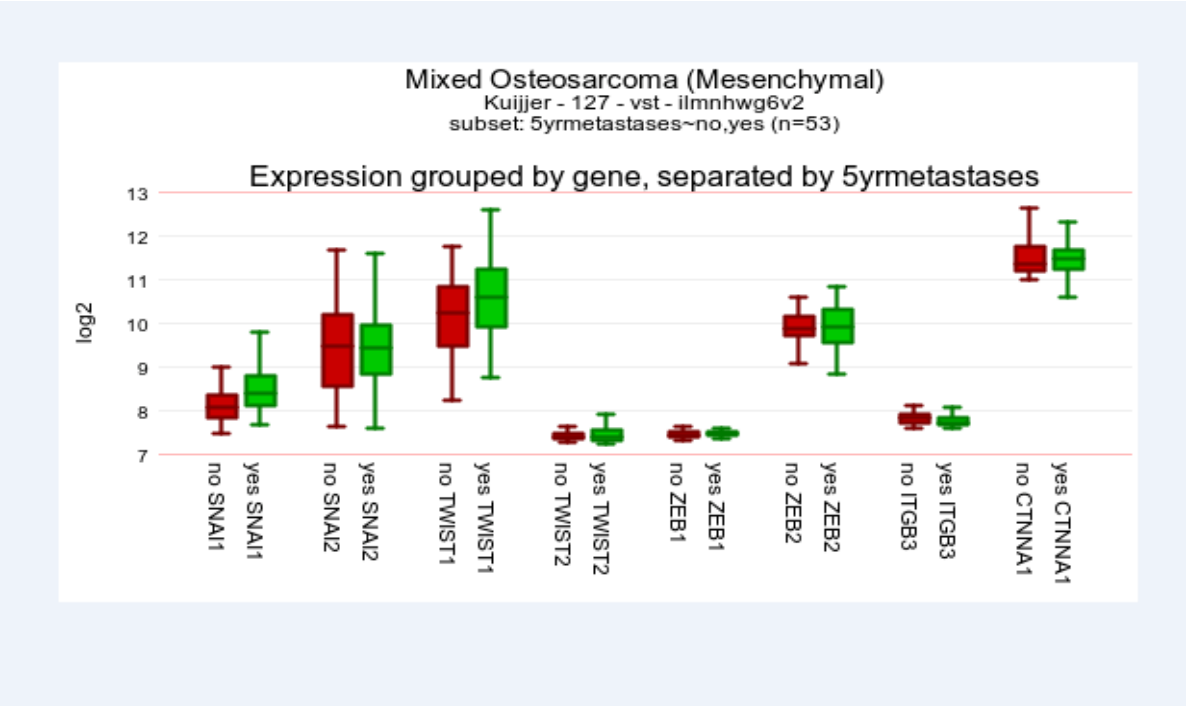


Figure 3: "Mixed Osteosarcoma (Genetic grouping)"

(Source: Self Developed)

From this above diagram, it can be illustrated that metastases are significantly low in ZEB1 and that low metastases indicate that there is a high effect on genes and a critical condition can be highlighted.

Result and discussion

SNAI 1 & 2

To induce EMT, Slug or Snail and TGF-beta signaling are utilized. It is also possible to achieve Snail and Slug expression using TGF-beta. Conversely, Slug and Snail are employed to induce the TGF-beta pathway in genes. TGF-beta and snail or slug impact dissections are thought to act mechanistically to induce EMT, according to Dhasarathy et al. (2011). In addition, MCF-7 cells are controlled following treatment with Snail or Slug adenovirus, DMSO, small molecule inhibitors SB431542, specific inhibitor of TGFBR2, and LY364947 in addition to TGFBR1 to generate TGFBR2 to a lesser degree. Dhasarathy et al. (2011) stated that the TGF beta pathway's impact on cell migration for enabling Slug and Snail induction is assessed by treating the cells with inhibitors, viruses, and DMSO.

In the event of advancement, malignant tumors originating from EMT and ZEB 1 continue to be related to the tumor pathogenesis. However, E-Cadherin is one of the key components where ZEB 1 can be utilized for either direct or indirect inhibition of E-cadherin production, according to Xu et al. (2017). E-Cadherin, which is next to molecules, can form protein dimers that help with "normal alignment of cells."

Conclusion

Consequently, it should be noted that an increase in osteosarcoma cells raises the risk of lung cancer through metastases. Therefore, maintenance must be used to lower hazards because survival rates also drop when osteosarcoma cell growth increases. Numerous cells are susceptible to contracting this illness.

In conclusion, it can be said that different kinds of cancer cells seen in a human body have E-cadherin cells.

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journal of recently scientific researcher's theory. – 2024. т. 2.№. 4. – с. 161-165.

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