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THE DIFFERENCE BETWEEN BRUSEIN-D LIGAND FROM MAKASSAR ETHANOLIC FRACTION (BRUCEA JAVANICA (L.) MERR) AND GEMCITABINE ON THE INHIBITION OF PANC-1 PANCREAS CARCINOMA GROWTH AND MUTANT P53 EXPRESSION

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Background Giving Brusein D or Gemcitabine to pancreatic carcinoma cells will re-infect genes that act as tumor suppressor genes. In Brusein D administration there will be activation of p38-MAPK, caspase 9 and caspase 3 as well as inhibition of NF- κ B which will stop the synthesis of pancreatic carcinoma DNA so that the cell will carry out cell degradation by apoptosis. In the administration of Gemcitabine, there will be tumor suppressor gene activation, p38-MAPK, which in turn will trigger cell degradation with the mechanism of apoptosis.

Methods PANC-1 pancreatic carcinoma cell cultures were divided into three groups. The first group was in control, the second group was treated with three repetitions of the dose of gemcitabine, the third group was treated with three repetitions of the Brusein D dose, then the number of mutant p53 was calculated in each group.

Results Mutant p53 expression levels in cultures of pancreatic carcinoma PANC-1 cells in vitro were the least in the Brusein D treatment 2 ug/ml (B 2), which average 12.7%, then Gemcitabine 2 ug/ml (G 2) which is an average of 16.7%, followed by Brusein D 1 ug/ml (B 1) which is an average of 22.0%, then followed by Gemcitabine 1 ug/ml (G 1) which is an average of 22.2%, followed by Brusein D 0.5 ug/ml (B 0.5) which is an average of 28.8%, then followed by Gemcitabine 0.5 ug/ml (G 0.5), which is mean average of 29.0%. And the highest level of mutant p53 expression was control, with an average of 51.3%.

Conclusions Brusein D ligand from an ethanolic fraction of Makassar Fruit (*Brucea javanica* (L.) Merr) has the inhibitory potential for mutant p53 expression so that it can be a candidate for the chemotherapeutic agent in cancer with mutations through the p53 pathway.

Abstract IDDF2019-ABS-0060 Figure 1 Brusein D inhibition on panc 1 pancreas carcinoma

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INCOMPLETE RADIOFREQUENCY ABLATION OF HCC PROMOTES INTRAHEPATIC METASTASIS AND STEMNESS IN A VEGFR1-DEPENDENT MANNER

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Background Approximately 50% hepatocellular carcinoma (HCC) patients recur within three years after radiofrequency ablation (RFA). Incomplete RFA of HCC could activate HIF/VEGF pathway to mediate malignant transition, and VEGF signaling was reported to enhance cancer stemness in skin cancer and Glioblastoma multiforme. We aimed to investigate the role of VEGF signaling on the process of incomplete RFA-related intrahepatic metastasis and stemness enhancement in HCC.

Methods HCC patient-derived xenograft (PDX) mice model and sublethal heat treatment cell model were established to mimic clinical setting of incomplete RFA. Cancer stem cell markers, MMPs, VEGF pathway, proliferation, migration and sphere were evaluated.

Results The expression of cancer stem cell (CSC) markers CD133, CD44, EpCAM was increased in tumor tissues with incomplete RFA from PDX mice compared to tumor tissues before RFA. Metastatic markers MMP2, MMP7 and MMP9 were also upregulated in tumor tissues with incomplete RFA, with increasing VEGFR1 and decreasing VEGFR2 expression. After sublethal heat treatment, enhanced cell migration ability was observed in HepG2, HCCLM3 and SMMC7721 cells, which coincided with an enhanced ability of sphere formation and upregulation of VEGFR1, CD133, CD44, and EpCAM. Further exploration revealed that HCC cells secreted more VEGF after heat-treatment. VEGF promoted the stemness and migration of HCC cells, which could not be suppressed by inhibiting VEGFR2. On the other hand, PlGF, the ligand of VEGFR1, significantly enhanced the stemness and migration of HCC cells. More importantly, blocking VEGFR1 reduced heat-induced stemness and migration, while inhibition of VEGFR2 did not reduce the stemness and migration of HCC cells with heat treatment.

Conclusions Sublethal heat treatment could increase the migration capability and stem cell-like phenotype of HCC cells. VEGFR1 played a critical role in such malignant transition after sublethal heat treatment, suggesting VEGFR1 may serve as a potential and promising therapeutic target for preventing recurrence after RFA.

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REDUCED EXPRESSION OF CIRC RNA HSA_CIRC_001888 IN GASTRIC CANCER AND ITS CLINICAL SIGNIFICANCE

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Background Circular RNAs (circRNAs) are a new class of endogenous noncoding RNAs. Owing to the special covalently closed loop structure without 5' end caps or 3' poly (A) tails, circRNAs are more stable and conserved than linear RNAs. Growing evidence shows that circRNAs play a crucial role in the occurrence and development of several human diseases,