Attn: Dear Dr. Aisyah Elliyanti
Medical Physics and Radiology
Faculty of Medicine, Universitas Andalas
Padang, West Sumatra, Indonesia

August 31th, 2017

Dear Dr. Aisyah Elliyanti,

It is our great pleasure to inform you that the 12th Asia Oceania Congress of Nuclear Medicine and Biology (AOCNMB 2017) to be held from October 5 to 7, 2017 in Yokohama, Japan.
in conjunction with:

The 57th Annual Scientific Meeting of the Japanese Society of Nuclear Medicine (JSNM)
The 37th Annual Scientific Meeting of the Japanese Society of Nuclear Medicine Technology (JSNMT)
The 7th Annual International Conference of the Asia Society of Nuclear Medicine (ASNMT)

Congratulations! Your abstract has been reviewed and accepted by the program committee of AOCNMB2017, as an oral presentation.

Submission Number : C000231
Title : Induction of Natrium Iodide Symporter Expression in Breast Cancer Cell Lines
Date : October 7th, 2017 11:20 -11:30
Venue : PACIFICO Yokohama 1-1-1, Minato Mirai, Nishi-ku, Yokohama, Japan

Your abstract will be published online in the program of AOCNMB2017.

We are sorry that AOCNMB is not providing any kind of financial assistance.
Thank you for your kind understanding.

Yours sincerely,

Tomio Inoue,
President, AOCNMB 2017
Professor, Yokohama City University Graduate School of Medicine

Tomohiro Kaneta,
Program Committee Chair, AOCNMB 2017
Yokohama City University Graduate School of Medicine

第57回
日本核医学会学術総会
The 57th Annual Scientific Meeting of the Japanese Society of Nuclear Medicine

第37回
日本核医学技術学会総会学術大会
The 37th Annual Scientific Meeting of the Japanese Society of Nuclear Medicine Technology

第12回アジア・オセアニア核医学会学術会議
The 12th Asia Oceania Congress of Nuclear Medicine and Biology

第7回アジア核医学技術学会国際会議
The 7th Annual International Asian Society of Nuclear Medicine Technology Conference

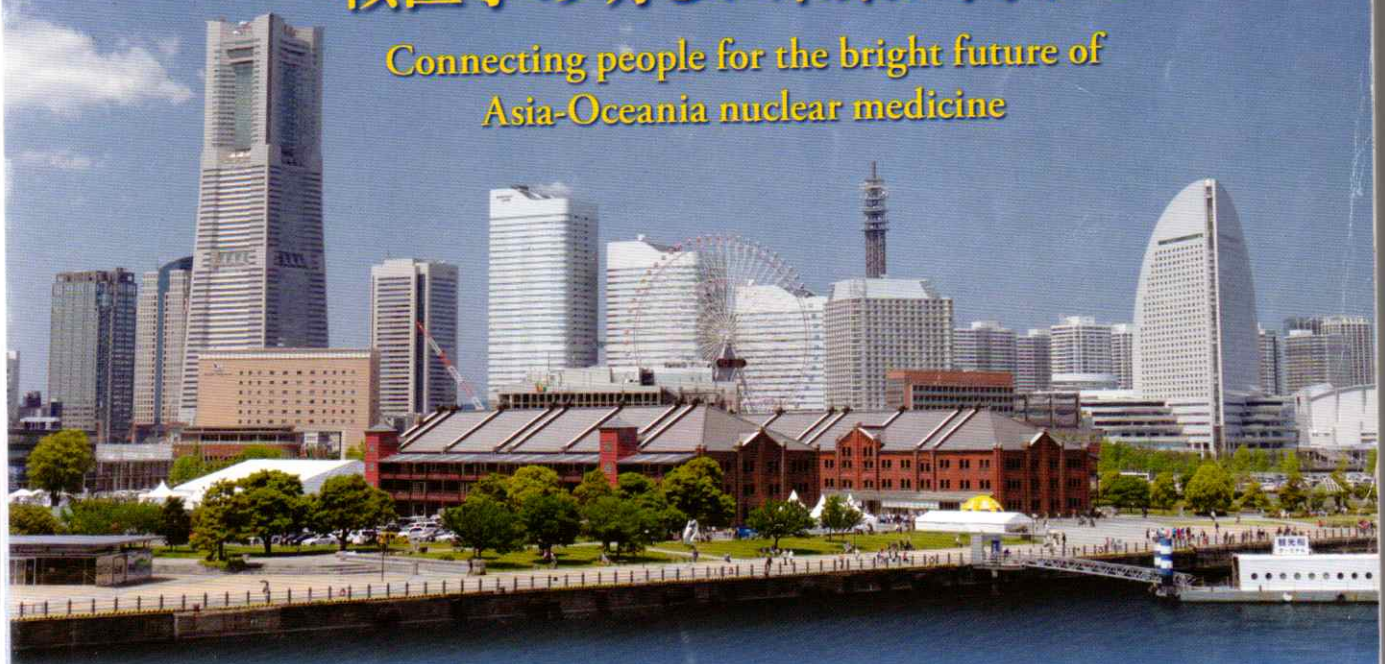
2017年10月5日(木)▶7日(土)
October 5 (Thursday) - 7 (Saturday), 2017

パシフィコ横浜
PACIFICO Yokohama

Program

核医学の明るい未来に向けて

Connecting people for the bright future of Asia-Oceania nuclear medicine



第57回 日本核医学会学術総会
第12回アジア・オセアニア核医学会学術会議
会　長　**井上 登美夫**

第37回 日本核医学技術学会総会学術大会
大会長　**渡邉 浩**

第7回 アジア核医学技術学会国際会議
会　長　**片渕 哲朗**

Tomio Inoue, Congress President of
The 57th Annual Scientific Meeting of the Japanese Society of Nuclear Medicine
The 12th Asia Oceania Congress of Nuclear Medicine and Biology

Hiroshi Watanabe, Congress President of
The 37th Annual Scientific Meeting of the Japanese Society of Nuclear Medicine Technology

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The 57th Annual Scientific Meeting of the Japanese Society of Nuclear Medicine
The 12th Asia Oceania Congress of Nuclear Medicine and Biology (AOCNMB 2017)

GREETING

"Sustainable Future Development of Nuclear Medicine in the Asia and Oceania Region"

Tomio Inoue MD
Congress President of JSNM and AOCNMB 2017
(Department of Radiology, Yokohama City University Graduate School of Medicine)

The reason that I determined "Connecting people for bright future of nuclear medicine in the Asia and Oceania region" as a key phrase of AOCNMB 2017 is that I believe Connecting people by academic activity of AOFNMB is the essential strategy to reach the bright future of nuclear medicine in the Asia and Oceania region. Historically, nuclear medicine has been sustainably developed since the late 1970s. However, main players in nuclear medicine have been changing by replacing newly developed alternative other imaging technology as US, CT, and MRI.

In the 2000s and 2010s, PET oncology seems to be most popular nuclear medicine in clinical practice by combination of FDG and PET/CT. In the 2010s, we are expecting popularization of theranostics as combination of PET/CT or PET/MR and radionuclide therapy using antibody/peptide labeled with Alpha or Beta emitter. The progress in nuclear medicine had been always supported by the combination of progress of many academic fields beyond nuclear medicine, including pharmacology, molecular biology, immunology, chemistry, engineering, computer science, and so on. In other ward, nuclear medicine essentially requires an interdisciplinary connecting people.

In 2015, General assembly of the United Nation adopts the following outcome documents of the United Nations summit for the adoption of the post-2015 development agenda: "Transforming our world: the 2030 Agenda for Sustainable Development". The Agenda that is a grand plan of action for people, planet and prosperity is not directly related to the future of nuclear medicine in the Asia and Oceania region, but we should consider and understand the grand concept for human being of the 2030 Agenda to make a plan of future development of nuclear medicine in the Asia and Oceania region until 2030. Among 17 sustainable development goals(SDGs) defined in the Agenda 2030, goal 3 is to ensure

healthy lives and promote well-being for all at all age which nuclear medicine could contribute. In the 2030 Agenda for sustainable developments, emerging countries should play a certain role for keeping sustainable developments as well as the advanced countries. The strategy of AOFNMB should be to adapt this scheme for sustainable developments of nuclear medicine in the Asia and Oceania region. As the nuclear medicine in East Asian countries has been rapidly developed with economic growth in each country in the 2000s, a certain different advanced field and technology of nuclear medicine in each developed country should be introduced into the developing countries under the scheme of the Agenda 2030 of UN. While the nuclear medicine leaders in developing country must play a role of stakeholder for spreading the technology in their own country and to keep the sustainable development goals. For keeping SDGs in the field of nuclear medicine, AOFNMB must go forward in the three directions of standardized education, standardization of NM examinations procedures, and innovative research of imaging devices as total-whole body PET/CT and/or novel radiopharmaceuticals. As standardization of NM examinations procedures, the concept and profiles of Quantitative Imaging Biomarker Alliance (QIBA) under RSNA might be important to keep sustainable developments in the field of nuclear medicine in the Asia and Oceania region.

GREETING

Hiroshi Watanabe RT, PhD
Congress president of JSNMT2017
(Japan Organization of Occupational Health and Safety, Yokohama Rosai Hospital)

As the congress president of the 37th Annual Meeting of Japanese Society of Nuclear Medicine Technology (JSNMT2017), I would like to express my sincere gratitude to the members and people concerned.

This annual meeting will be held on October 5th (Thursday) to 7th (Saturday), 2017, in Yokohama. And, this annual meeting will be held jointly with the 57th Annual Scientific Meeting of the Japanese Society of Nuclear Medicine (JSNM), the 12th Asia Oceania Congress of Nuclear Medicine and Biology (AOCNMB) and the 7th Annual International Meeting of Asian Society of Nuclear Medical Technology (ASNMT).

The theme of this annual meeting is "Connecting people for the bright future of Asia-Oceania nuclear medicine". The environment surrounding the nuclear medicine is evolving day by day. Therefore, under such circumstances, we plan for various discussions with members and participants for the bright future of nuclear medicine, such as the JSNM and JSNMT Joint Symposium, the JSNMT Symposium, the basic course, the new image contest and the JSNMT and ASNMT joint international session etc. Also, the joint meeting of the JSNM and the JSNMT is the 10th year. We would like to collaborate with JSNM organizing committee members and hold a wonderful meeting for further development of nuclear medicine.

Furthermore, the Yokohama Minatomirai district where the venue is located is a worldwide tourist destination. There are many famous tourist sites such as Yokohama Red Brick Warehouse, Yokohama Landmark Tower, Yokohama Chinatown. Please enjoy sightseeing as well.

Finally, this annual meeting will be held in Yokohama (in Kanagawa prefecture) for the first time in a while. Therefore, we receive support from many people such as the Kanagawa society of nuclear medicine and the Kanto regional association of nuclear medicine technology, etc,. We appreciate all of you for your cooperation. we sincerely looking forward to seeing all of you at JSNMT2017 in Yokohama in 2017.

The 7th Annual International Conference of Asian Society of Nuclear Medicine Technology

President's Greeting

"Expect for nuclear medicine technology in Asia"

Conference Chair; Tetsuro Katafuchi, RT, PhD
(Gifu University of Medical Science)

We are pleased to announce that the 7th Annual International Conference of the Asian Society of Nuclear Medicine Technology (ASNMT) will be held at PACIFICO Yokohama on October 6, 2017. It is a great honor for us to host the conference.

ASNMT holds the annual conference for mutual exchange in academic and clinical nuclear medicine technology since 2011. Our objective is to contribute to the development of nuclear medicine technology in the Asian region through the many technologists who attend the annual conference from various countries.

The 7th ASNMT is jointed with the 57th Annual Scientific Meeting of the Japanese Society of Nuclear Medicine, the 37th Annual Meeting of the Japanese Society of Nuclear Medicine Technology and the 12th Asia Oceania Congress of Nuclear Medicine and Biology, which congresses will be precious meetings for academic exchanges. This conference program plans the oral presentations and poster presentations in academic study, and besides, special speaker is invited lecturer from Australia.

On behalf of the steering committees of ASNMT, I would like to ask you that you understand the purpose of ASNMT and give us great supports and guidance to make the conferences success.

The 57th Annual Scientific Meeting of the Japanese Society of Nuclear Medicine
The 12th Asia Oceania Congress of Nuclear Medicine and Biology (AOCNMB 2017)

Date October 5(Thursday) – 7(Saturday), 2017

Venue PACIFICO Yokohama
1-1-1 Minatomirai, Nishi-ku, Yokohama 220-0012, Japan

In conjunction with
The 37th Annual Meeting of the Japanese Society of Nuclear Medicine Technology
The 7th Annual International Conference of the Asian Society of Nuclear Medicine Technology

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President Tomio Inoue, MD, PhD
Secretary General Izumi Koike, MD, PhD
Program Committee Chair Tomohiro Kaneta, MD, PhD

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Yansong Lin (Peking Union Medical College Hospital, China)
Zhaohui Zhu (Peking Union Medical College Hospital, China)
Zvi Bar-Sever (Schneider Children's Medical Center of Israel, Israel)

RI therapy　Saturday Oct.7 10:00-11:00, Room 7

Chair : Suresh C. Srivastava (Brookhaven National Laboratory, USA)
Tetsuya Higuchi (Department of Diagnostic Radiology and Nuclear Medicine, Gunma University)

BM3VIIC-01 Bevacizumab radioimmunotherapy (RIT) in triple-negative breast cancer (TNBC) xenograft
(Radiology and Nuclear Medicine, Gunma University) Ryan Yudistiro

BM3VIIC-02 ^{177}Lu-hydroxyapatite (Lu-177 HA) in Radiosynovectomy of knee joints due to Rheumatoid arthritis.
(Department of Nuclear Medicine and PET/CT, Kovai Medical Center and Hospital, India) Kamaleshwaran Koramadai Karuppusamy

BM3VIIC-03 Preclinical study of α-RIT against liver metastasis of gastric cancer
(Graduate School of Medical and Pharmaceutical Sciences, Chiba University) Huizi Keiko Li

BM3VIIC-04 Evaluation of Radiation Exposure Rate after I-131 Treatment of Patients
(Division of Nuclear Medicine,Chi Mei Medical Center, Taiwan) Chien- hua Lu

BM3VIIC-05 Efficacy of 1110 vs. 3700 MBq RAI in Remnant Ablation of Low Risk Dtc: A Meta-Analysis
(Philippine Heart Center, Philippine) Henry Gochoco Canizares

Thyroid, Breast　Saturday Oct.7 11:00-11:50, Room 7

Chair : Mei Tian (Zhejiang University)
Sze Ting Lee (Austin Hospital, Austrailia)

BM3VIID-01 Response prediction of neoadjuvant therapy by dedicated-breast PET: compared with MR volumetry
(Diagnostic Imaging and Nuclear Medicine, Kyoto University Graduate School of Medicine) Masako Kataoka

BM3VIID-02 The Effect of FDG-PET/CT in Response of Breast Cancer Therapy
(Faculty of Paramedicine, Semnan University of Medical Sciences, Semnan, Iran) Mohsen Shoja

BM3VIID-03 Induction of Natrium Iodide Symporter Expression in Breast Cancer Cell Lines
(Medical Physics and Radiology, Universitas Andalas, Singapore) Aisyah Elliyanti

BM3VIID-04 Importance of isolated raised thyroglobulin antibody in follow up and management of differentiated thyroid cancer
(Nuclear Medicine, Tata Medical Center, India) Ray Soumendranath

BM3VIID-05 Can ^{18}F-FDG-PET predict ^{131}I therapeutic response in metastatic differentiated thyroid carcinoma?
(Department of Diagnostic Radiology and Nuclear Medicine, Gunma University) Xieyi Zhang

InductionofNatrium Iodide Symporter Expression in Breast Cancer Cell Lines

Aisyah Elliyanti[1], AndaniEka Putra[2],Yunia Sribudiani[3], Noormartany[4], Johan S.Masjhur[5], Tri Hanggono Achmad[3]

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[2] Department of Microbiology, Faculty of Medicine, UniversitasAndalas.

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[4] Department of Clinical Pathology, Faculty of Medicine, UniversitasPadjajaran

[5]Department of Nuclear Medicine and Molecular Imaging, Faculty of Medicine, UniversitasPadjajaran.

Natrium iodide symporter (NIS) is an iodide co-transporter, which plays a pivotal role in radioiodine uptake in breast cancer cells. The level of NIS expression in breast cancer tissues was reported to be varied between studies. Adenosine triphosphate (ATP) and epidermal growth factor (EGF) are proliferative agents which activateextracellular signal-regulated kinase (ERK). The signaling pathway has been known, play an important roles in NIS expression regulation. The aim of this study is to investigatethe effect of ATP, EGF and combination of those two to the NIS expression in MCF7 and SKBR3 cell lines.

MCF7 cell line is representing the luminal type of breast cancer and SKBR3 cell line is representingthe human epidermal receptor 2 (HER2) type.Hacat cell line, a non-cancer cell, is used as control. Cells were treated with ATP, EGF and combination of those two for 6, 12 and 24 hours. The expression of NIS *mRNA*was measured throughquantitative-reverse transcription-polymerase chain reaction (qRT-PCR). The NIS protein expression was confirmed by immunocytofluoresence.

Natrium iodide symporterwas expressed in SKBR3and in Hacat cells with or without ATP and EGF treatment. However the same treatment did not induce NIS expression in MCF7 cells .The combination of ATPand EGF treatment for 24 hours enhanced the level of NIS*mRNA*expression in SKBR3 cell line by 1.6 folds compared to that of untreated cells ($p<0.05$).It also increased NIS protein expression at membrane cells in SKBR3 cell line.

The level of NIS expression is different among subtypes of breast cancer cell lines. ATP and EGF combination treatment increases NIS*mRNA*and protein expression in SKBR-3cells line.

Keywords: Natriumiodide symporter, Breast cancercell lines, Epidermal growth factor, Adenosine triphosphate

Introduction

Natrium Iodide Symporter is a plasma membrane glycoprotein. It transports two ions of natrium (Na^+) and one of iodide (I^-) and maintained by Na^+/K^+ ATPase[1,2].In thyroid cells, NIS plays a pivotal role to accumulate an iodine. Additionally, NIS is also expressed in breast cancer tissue and has been considered as a potential target

for radioiodine therapy. However, NIS expression in breast cancer tissues had been reported to be varied between studies. Furthermore, molecular mechanism of NIS expression in breast cancer remains unclear. Interestingly, it has been reported that NIS is highly expressed in invasive breast cancer tissues. Study by Tazebay*et al* reported that indeed there is a correlation between NIS expression and malignant transformation of human breast tissue[3,4].

Other than the variation of NIS expression level between molecular subtypes of breast cancer, the location of NIS expression is another factor that may influence the uptake of radioiodine by breast cancer cells. Natrium Iodide Symportersupposed to be localizedat membrane cell instead in the cytoplasm to be fully functional as iodine co-transporter[5,6].Several agents were used to increase NIS expression in breast cancer cells. Theeffectof those agents had been proven could increase radioiodine uptake and cells susceptibility toward the treatment. In T47D cell line, epidermal growth factor (EGF) treatment was reported to have anincrease inNIS expression at membrane cell[7].Another study reported that a combination of ATP with all-trans-Retinoid Acid (tRA) and hydrocortisone has increased NIS protein expression and cell membrane targeting in MCF7 cells[8].

In this study, we examined the effect ofEGF and ATP treatment forNIS *mRNA* and protein expressions in SKBR3 and MCF7breast cancer cell lines. MCF7 and SKBR3 cell lines are representing the luminal and HER2 type of breast cancer respectively[9].Hacat cell line, a human keratinocyte cell lines, is used as a control.

Material and Methods

Cell lines and culture conditions

SKBR3, MCF7 and Hacat cell lines were used in this study. SKBR3was obtained from the American Type Culture Collection (ATCC). MCF7 and Hacat cell lines were kindly provide by Dr. Ahmad Fariedfromfaculty of Medicine, UniversitasPadjadjaran, Bandung-Indonesia. MCF7and Hacat cells were cultured in RPMI 1640 medium(Sigma-Aldrich). SKBR3 was cultured in Mccoy's 5A medium(Sigma-Aldrich). Both cell culture mediums were supplemented with 10% fetal bovine serum (Sigma-Aldrich), 1% Penicillin, 1% Streptomycin and

1% amphotericin B. The cells were incubated at 37^{o}C and supplied with 5% of carbon dioxide (CO_2) until 80% confluence. The cells were incubated in serum-free medium overnight, and followed by treatment of EGF 50ng/ml (Abcam #ab9697), ATP 100μM (Sigma-Aldrich # 1388), anda combination of EGF and ATP, for 6, 12 and 24 hours. The cells without any treatment were used as a control

Quantitative Real-time reverse transcriptase –PCR (qRT-PCR)

The cells were harvested at the appropriate time pointsby trypsinized, and then followed by centrifuged at 1000 rpm for a period of 4 minutes. The total RNA was isolated by using RNeasy mini kit (Qiagen #74106) following the manufacturer's instructions. RNA was quantified using Nanodrop 2000and 5 ngof RNA was reverse transcribed and analyzed by one step real-time quantitative PCR using Rotor Gene Quantitect probe RT-PCR (Qiagen # 204443) using NIS and beta actin primers. The NIS expression fold change of treated cells to those untreated was analyzed using a method describe by Livak et al[10]. Three independent qPCR assays were conducted in triplicate.

Immunocytofluoresence

The cells were seeded on coverslips in awells of a 24-wells culture plate and fixated by 4% paraformaldehyde for 15 minutes. This was followed by incubation with protein blocking agent fluorescein-isothiocyanate (FITC) for 15 minutes. The cells were rinsed twice with an ice-cold PBS and followed by an overnight incubation with 2μg/ml rabbit polyclonal antibody anti-NIS(Abcam,#ab83816) at 4^{o}C.The cells were rinsed three times with PBS and incubated at room temperature with Goatanti-Rabbit IgG secondary polyclonal antibody, with dilution 1:1500 (Abcam,# ab6716)for one hour. The cellswere rinsed three times with PBS.The coverslips were placed over slides and mounted with fluoroshieldcontaining DAPI. The slides were inspected under immunofluorescense microscope (Olympus BX51) with 200x magnification.Cells which only incubated with secondary antibody were used as negative control.

Statistical analysis

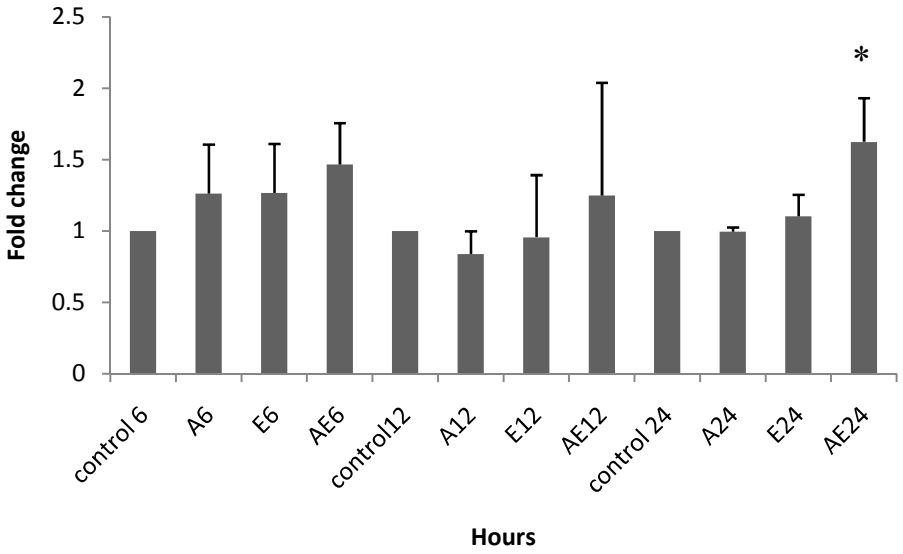
Collected results are expressed as mean ± SD. Data were analyzed using ANOVAmethod followed by Tukey test.SPSS was used in all analyses. P<0.05was considered statistically significant.

Results

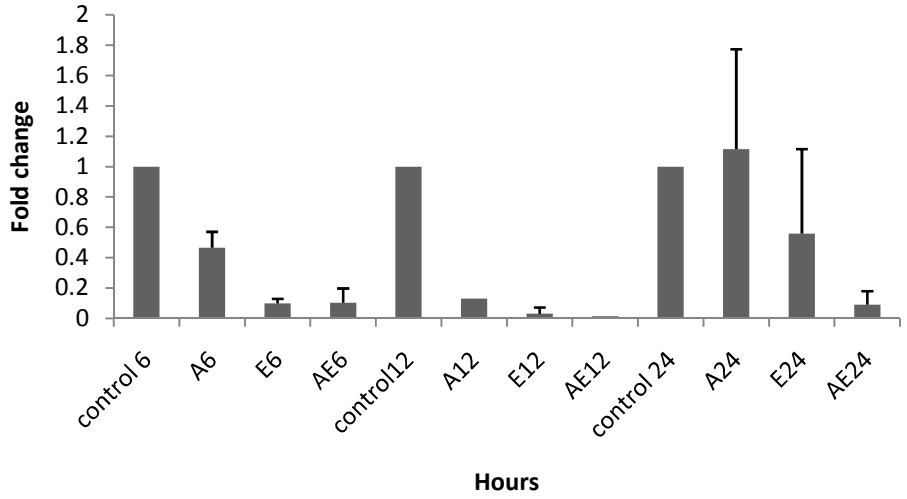
Effect of EGF and ATP treatment on NIS *mRNA*expression

We observed that NIS *mRNA*isexpressed in SKBR3 and Hacat cell lines but not in MCF7. In order to examine the effect of EGF and ATP on NIS expression level, we treat all cell lines with ATP, EGF and the combination of both.

The levels of NIS *mRNA* expression, after treatment by EGF, ATP or the combination of both for 6 and 12 hours were not significantly different from those of untreated cells (figure 1A). However, the treatment by a combination of ATP and EGF for 24 hours increases the level of NIS *mRNA* expression by 1.6 fold higher than that of the untreated cells (1.6241 ± 0.3, $p<0.05$). The treatment of ATP, EGF and the combination of both in Hacat cells do not increase the level of NIS *mRNA* expression (figure 1B).



1A



1B

Figure 1:(A)represents the effect of ATP (A), EGF (E) and a combination of ATP and EGF (AE) for 6, 12 and 24 hours treatment on NIS *mRNA* expression. The combination of ATP and EGF (AE) for 24 hours treatment increases NIS *mRNA* expression of SKBR3 cell significantly when comparedto untreated cells,$P<0.05$.*(*B) NIS *mRNA* expression of Hacat cells remains unchangedfor both treated and untreated cells, $P>0.05$.

Effect of EGF and ATP treatment on NIS protein expression

Results of immunoflourences showed that NIS protein expressin SKBR3 (figure 2). The NIS expression in this cellsismostly found in cytoplasm. The treatments of EGF and the combination of both for 12 and 24 hours increase NIS protein expression at membrane cell(figure 2B-C). The cells which receive ATP only for 24 hours show a slight increase in NIS protein expression at membrane cell.

Moreover, NIS expression can be detected in Hacat cells with and without treatments.Treatmentsof these cells by ATP, EGF and the combination of both induceincreasing of the expression NIS protein only in cytoplasm (figure 3). On the other hand, we cannot detect NIS protein expression in MCF7 cell line. This result is in agreement with the results of qRT-PCR.

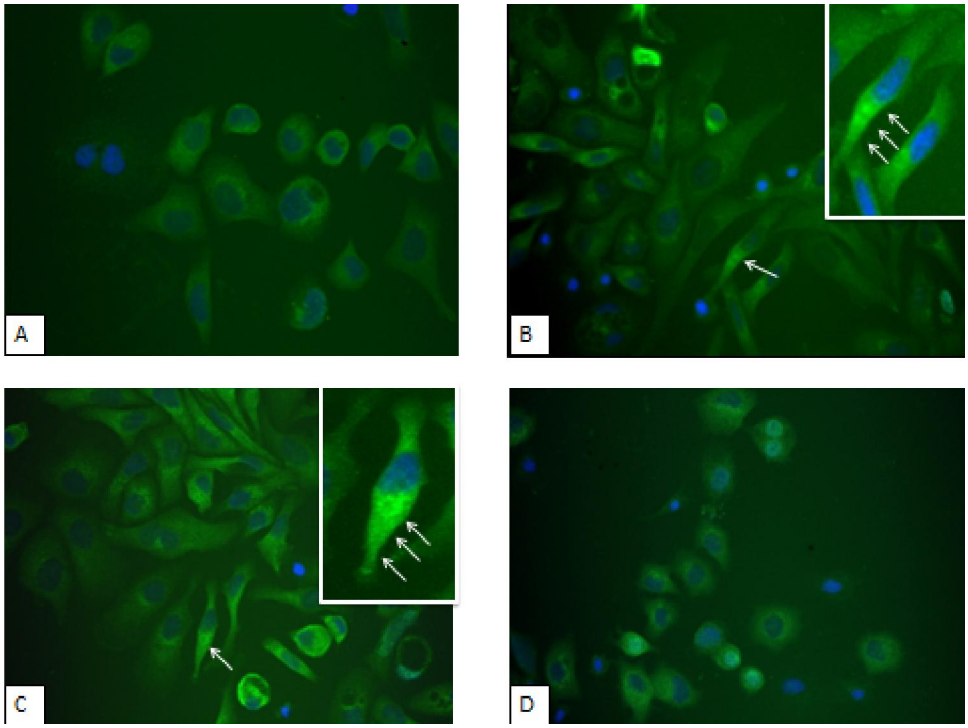


Figure 2: Immunoflouresence staining using primary antibody against NIS in SKBR3 cell line (green) and merging with DAPI staining (blue) at 200x magnification. (A,B,C)NIS is expressed after 24 hourstreatments with ATP, EGF and the combination of both respectively.NIS expression in SKBR3 cells increase both in cytoplasma and membrane after 24 hours treatment by both ATP and EGF. (D)untreated cells

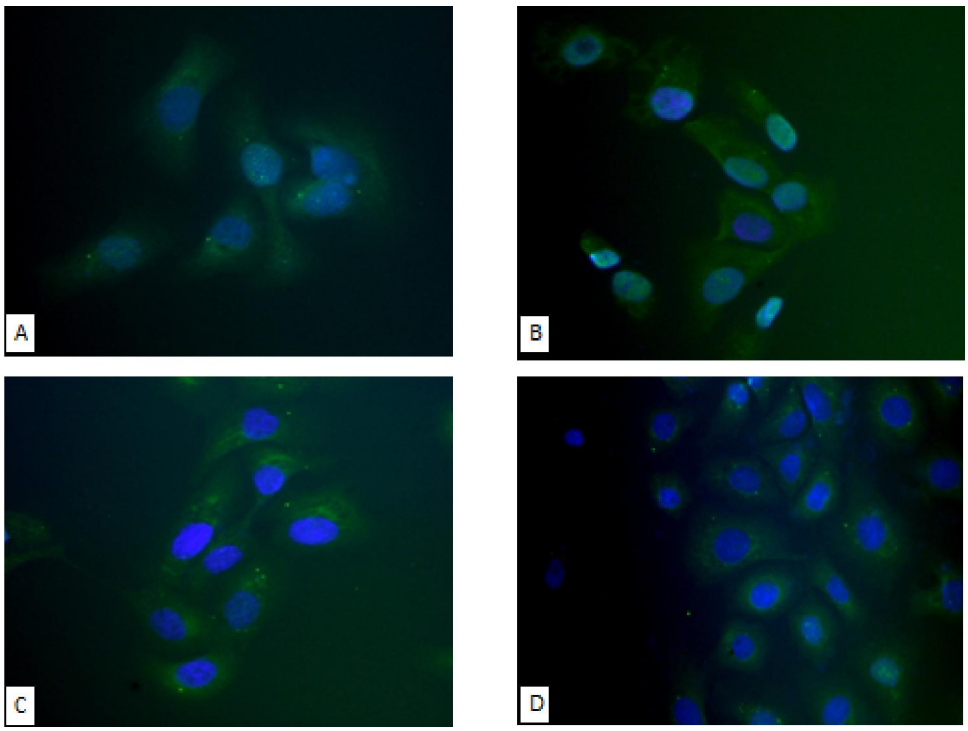


Figure 3: Immunoflouresence staining using primary antibody against NIS in Hacatcell line (*green*) and merging with DAPI staining (blue) at 200x magnification.(A,B,C)NIS is not expressed after 24 hourstreatment of ATP, EGF and the combination of both, respectively and (D) untreated cells. NIS protein expression of cells that are either treated or untreated are expressed in cytoplasm.

Discussion

The expression of NIS in extra-thyroid tissueshas been reported in some previous studies, however the restuls were vary. These findings have been considered as potential for radioiodine therapy in extra-thyroid tumor, including breast cancer. A study by Tazebay, et al reported that NIS was expressed in more than 80% of invasive breast cancer tissues.Another study by Wapnir,et alreported that the expression was found in 76% of invasive breast cancer tissues. Studies by other groups reportedthat 34% out of 44 breast cancer tissues express NIS. They also reported that65.5% out of 23 triple negative breast cancer tissuesexpress NIS[11,12,13].

In this study, we find that NIS *mRNA* and protein are expressed only in SKBR3 cells. Furthermore, the expression of NIS is not detectedin MCF7 cells. As previously published studieson MCF7 cells for the detection of NIS expression, they reported that adding retinoid acid (RA) is mandatory[8,14]. Thus, it can safely be assumed that NIS expression in MCF7 is RA-pathway dependent. Till date, the molecular mechanisms of NIS expression in breast cancer are not clearly defined. So that, further studieson targeted radioiodine therapy for breast cancerare needed.Meanwhile, it is important to determinethe molecular breast cancer typeswhich express NIS as potential candidate to receive radioiodine.

It has been established that MCF7 cell line type of breast cancer model is luminal A,with estrogen and progesteronereceptors positive (ER^+/PR^+) and HER2 receptor negative ($HER2^-$). SKBR3 is a breast cancer cell line with HER2 receptor positive ($HER2^+$),estrogen and progesterone receptors negative (ER^-/PR^-)[9,15].A study by Oh et al,reported that NIS expression is not correlated with the level of hormonal receptors, such as ER/PR.Hormones that regulate NIS expression in breast lactating stage may not play a role in breast cancer[16]. Moreover, a study by Dohan et al reported that prolactin, oxytocin and estrogen did not induce NIS expression[8]. Theefficacy of radioiodine therapy for breast cancer will be likely dependent on the level of NIS expression at the membrane cell. Therefore, stimulating of the NIS expression at membrane cell will increase iodine uptake.Several agents are used to increase NIS expression, such as retinoic acid, hormones and proliferative agents[2,7,17]. Epidermal growth factor and ATP are classified into proliferative agent. Binding EGF with EGF receptor will stimulate the tyrosine kinase activityand induce cell proliferation[18]. Another study, by Tazebayet al, reported that there is a correlation between NIS expression and malignant transformation of human breast

tissue[3,4]. This leads us to speculate that one of the molecular mechanism to induce cells proliferation is by EGF-EGFR pathway to up-regulate the NIS expression.

In this study, we observed that NIS *mRNA* expression and protein localization at membrane cell increases by the combination of ATP and EGF treatment in SKBR3 cells (*Figure 2*). Treatment of ATP and EGF alone do not increase the level of NIS *mRNA*; but, increases the membrane NIS protein after 12 and 24 hours treatments. A Study by Jung KH et al reported that EGF treatment augmented NIS mRNA and protein expression in T47D cell line,which transfectedwith NIS. However, further investigation is needed to understand the molecular mechanism of NIS stimulation in HER2 type by EGF and ATP treatment.

In our study, we are unable to detected NIS expression in MCF7 cells with or without treatment. These cells are negative or express low level of EGF receptors[19]. This may explain the absence of NIS expression under EGF induction in MCF7cells. However, EGF is able to augmented NIS expression in MCF7 cells which is transfectedNIS, even though the cells do not have EGF receptors. Further studies are still required to be performed in order to elucidate the mechanism of NIS expression in breast cancer and the differences with NIS expression between the molecular subtypes of breast cancer. Additionally, NIS expression can be detected in Hacat cells, even though the expression is within the cytoplasm. Neither ATP nor EGF treatment will increase NIS expression in Hacat cells.

Conclusion

The level of NIS expression varies among the different subtypes of breast cancer cell lines. MCF7 cell line is representing the luminal typeof breast cancer do not express NIS as good as SKBR3cell line, which representsthe HER2 type. This type might be suitable to receive radioiodine therapy as those cells expressing NIS.A combination treatment of EGF and ATP increases the expression of NIS *mRNA* andprotein at membranein SKBR3 cells.

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Conflict of Interset Statement

No potential conflicts of interest are disclosed

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Thyroid, Breast

Chair: Mei Tian(Zhejiang University), Sze Ting Lee(Austin Hospital, Austrailia)
Sat. Oct 7, 2017 11:00 AM - 11:50 AM Conference Room 7 (414+415, Conference Center 4F)

[BM3VIID-03]Induction of Natrium Iodide Symporter Expression in Breast Cancer Cell Lines

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Adenosine triphosphate (ATP) and epidermal growth factor (EGF) are proliferative agents which activate extracellular signal-regulated kinase (ERK). They are hypothezed play a role in Natrium iodide symporter (NIS) expression regulation. The aim of this study is to investigate the effect of ATP, EGF to the NIS expression.
MCF7 and SKBR3 cell lines are used in this study and Hacat is used as control. Cells were treated with ATP, EGF and combination of those two for 6, 12 and 24 hours. The expression of NIS *mRNA* was measured through quantitative-reverse transcription-polymerase chain reaction and NIS protein was confirmed by immunocytofluoresence.
Natrium iodide symporter was expressed in SKBR3 cells with and without treatments. The combination of ATP and EGF treatment enhanced the level of NIS *mRNA* expression in SKBR3 cell line by 1.6 folds compared to that of untreated cells ($p<0.05$). It also increased NIS protein expression at plasma membrane.
ATP and EGF combination treatment increases NIS *mRNA* and protein expression in SKBR-3cells line.