Terahertz wave activates filamentation of actin

A novel possibility of manipulating cellular functions

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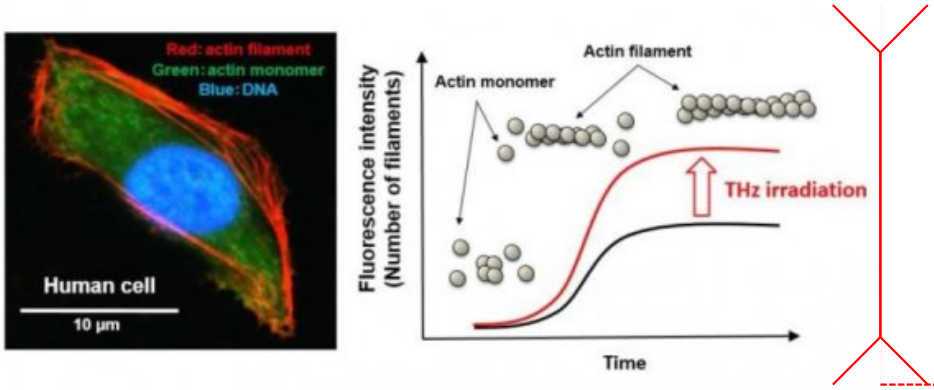


Actin forms filaments in cells and plays essential roles in multiple cellular functions including cell motility, cell division, and gene expression (left). By monitoring the polymerization reaction of purified actin protein **under THz irradiation, it was found that THz wave activates the filamentation of actin.** A team of researchers have discovered that terahertz (THz) wave irradiation activates the filamentation of actin protein. Drs. Shota Yamazaki and Masahiko Harata (Graduate School of Agricultural Science, Tohoku University); Dr. Yuichi Ogawa (Graduate School of Agriculture, Kyoto University); Dr. Hiromichi Hoshina (THz imaging and the sensing team at RIKEN); and Dr. Toshitaka Idehara (FIR-UF at University of Fukui) **have made this important discovery, which offers a new possibility for the manipulation of cellular functions** Due to the recent development of high **power THz (1012 Hz) wave sources, many researchers have begun to explore its application for material manipulation**. One of the advantages of **THz wave irradiation is its lower photon energy as compared to visible light**. **Therefore, THz wave prevents the ionization of molecules. THz wave enables "soft" manipulation of macromolecules such as proteins, enabling changes to their higher-order structure without damaging the samples. Actin forms filaments through its polymerization in cells, and functions as a major component of cellular architecture. Actin plays a central role in various cellular functions, including wound healing and the metastasis of cancer cells. In addition, a portion of actin exists in the cell nucleus and regulates gene regulation. For example, actin is required for gene reprograming, which is required for establishing iPS (induced pluripotent) cells. In this research, the polymerization reaction of purified actin protein was monitored under irradiation of THz wave, and it was found that**

Comment [i]: **THz range, lies between infrared and microwave radiation in the electromagnetic spectrum, and it shares some properties of each. Specifically, it travels in a straight line and is nonionizing. The THz spectral range**

Comment [i]: **We found that the THz and bulk heated cells express a similar number of DEGs, 628 and 556 genes, respectively---- differentially expressed genes (DEGs)**

Comment [i]: One aspect of what this is supposed to do--- Our approach is motivated by the fact **that cells activate specific genes and intracellular signaling pathways when exposed to different stressors. Thus, if THz radiation**

the THz wave activates the filamentation of actin. Actin governs various functions of cells. Therefore, a variety of drugs have been developed for controlling actin filamentation, and applications of these drugs for medical purposes have been explored. However, **these drugs are inefficient in their delivery into, and clearance from, cells**. **THz irradiation is a non-invasive method and could overcome these identified problems in drugs. THz wave is expected to become a novel tool for the manipulation of cellular functions through modifying actin filamentation**. This research team is now trying to understand the basic mechanism of the THz assisting filamentation to extend this technology to various proteins so that THz irradiation can be widely applied to various biological technologies.-**Story Source-**Materials provided by **Tohoku University**. **Journal Reference**-Shota Yamazaki, Masahiko Harata, Toshitaka Idehara, Keiji Konagaya, Ginji Yokoyama, Hiromichi Hoshina, Yuichi Ogawa. **Actin polymerization is activated by terahertz irradiation**. *Scientific Reports*, 2018; 8 (1) DOI: 10.1038/s41598-018-28245-9 --Tohoku University. "Terahertz wave activates filamentation of actin: A novel possibility of manipulating cellular functions." ScienceDaily. ScienceDaily, 30 August 2018. <www.sciencedaily.com/releases/2018/08/180830095339.htm>.

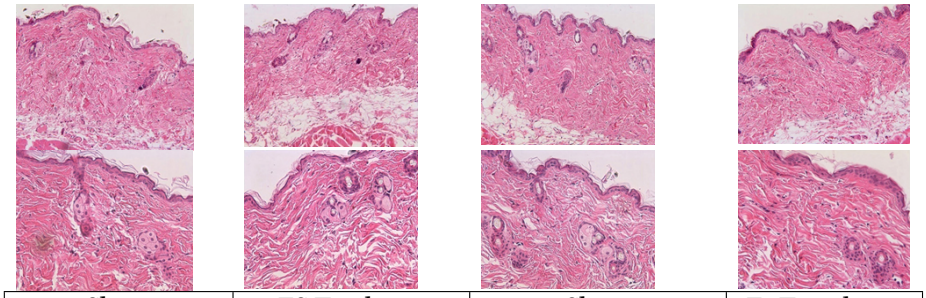
We exposed the back skin of 8-week-old male C57BL/6 mice to the fs-THz beam and examined the histological and molecular biological changes. Briefly, the hair on the back of the mice was clipped and they were positioned in the customized acryl restrainer manufactured for this experiment. After taking a precise position with the visible beam in targeting the spot, the back, the skin (size, 1×1 cm2) was exposed to the fs-THz beam for 1 hour. Accumulated energy in the targeted area for 1 hour was calculated as approximately 1.15 J/cm2.

Skin biopsy samples were taken at 1 and 24 hours after exposure

However, the quantitative real-time polymerase chain reaction analysis for the genes screened through microarray analysis reveals that some genes in the fs-THz-irradiated mice were either biologically activated or suppressed. For instance, the gene transcription of substance P (SP), a neuropeptide that is released from the C and Aδ fibers and is involved in local inflammation, including dermatoses, decreased significantly at 24 hours after exposure (Fig. 2A**). On the contrary, the transcription of calcitonin gene-related peptide, another neuropeptide that is also associated with neurogenic inflammation in eczema, increased significantly in fs-THz-irradiated mice**

Comment [i]: **THz exposure group than for the bulk heated group, 75% versus 55%. Interestingly, many of the identified genes encode for proteins involved in plasma membrane function, including ion channels, transmembrane transporters, and G-protein receptors membrane of virtually every mammalian cell. Ion channels open or close in**

Comment [i]: **Skin biopsy samples were taken at 1 and 24 hours after exposure. Mice in the sham group were treated in the same manner except for the fs-THz beam exposure. Skin samples were stained with hematoxylin and eosin for histological assessment. We found that fs-THz irradiation did not induce any obvious histological**



Sham	FS Terrhertz	Sham	Fs Terrahertz

Histological observations on the back skin of C57BL/6 mice exposed to the femtosecond-Terahertz (fs-THz) beam for 1 hour (H&E; ×200 and ×400). Skin samples were biopsied at 1 and 24 hours after exposure

THz radiation may be preferentially coupled to and selectively absorbed by interfacial water that is bound to surface of biomolecules on the plasma membrane [11]. This direct coupling mechanism is hypothesized to cause a localized temperature rise on the membrane surface, which result in microthermal effects that are not quantifiable with modern dosimetric tools

Specifically, the magnitude of expression for KCNA2 and CACNA1G increased linearly with THz stimulus. Indeed, this finding is not surprising given the fact that the response of mammalian cells is typically closely related to the magnitude of the stimulus or stressor [12, 13]. In marked contrast to the above genes, we also found that several genes exhibited either maximal expression levels for the shortest THz exposure,and/or showed reduced expression levels for the longer exposures

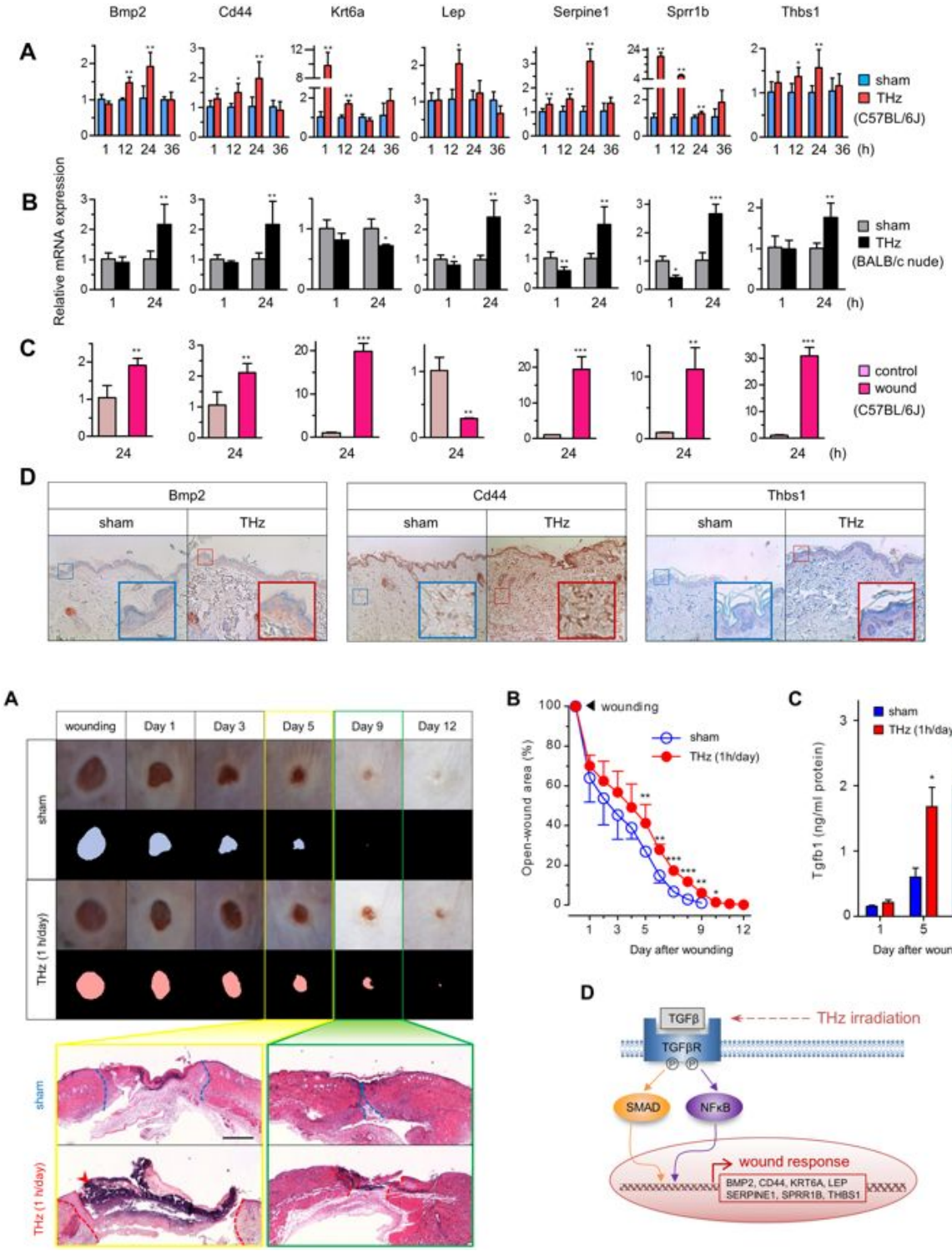
THz exposure (e.g., SLC6A13, SLC26A7). The SLC family is a large group of membrane transport proteins that are responsible for transporting organic and inorganic molecules both in and out of cells. The data provided here suggests that THz radiation ay impact the balance of these molecules

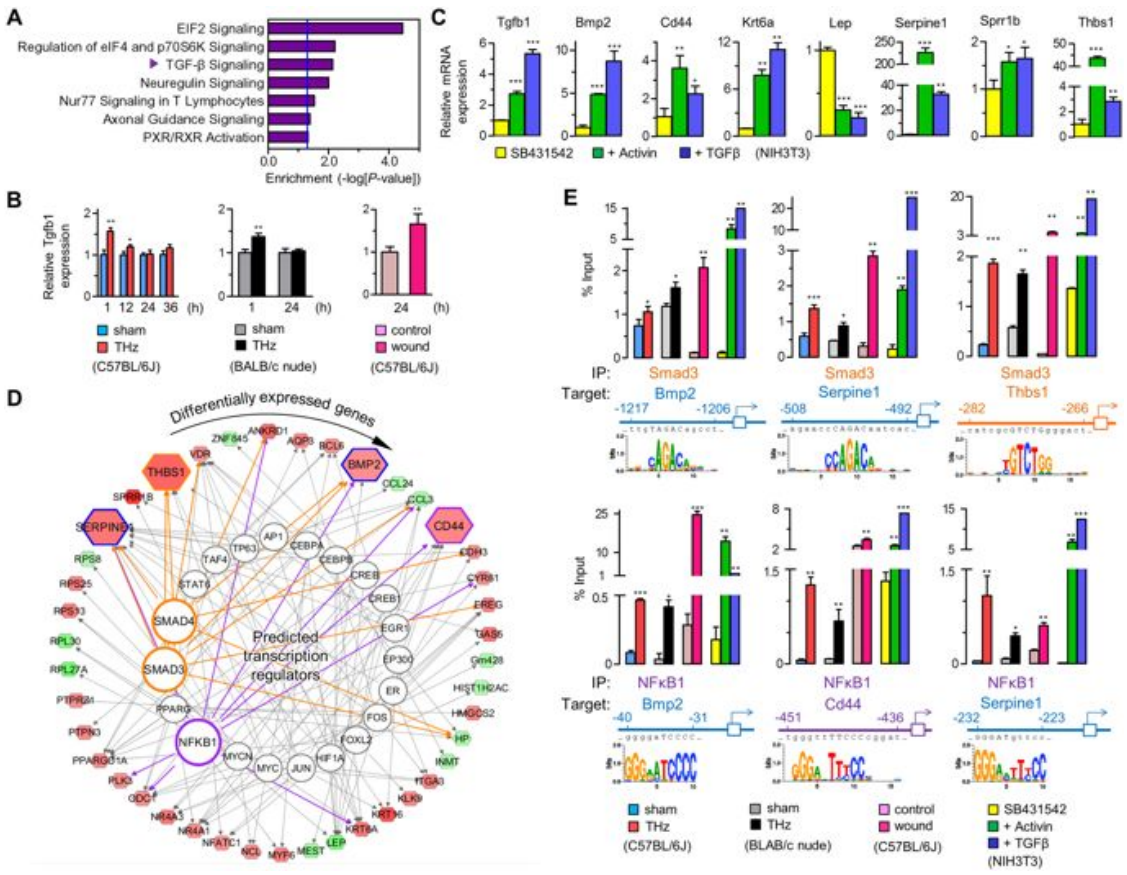
Fig. 2. Gene expression in the femtosecond-Terahertz (fs-THz)-irradiated mouse skin. The back skin of C57BL/6 mice (sham, n=4;fs-THz, n=5; A~D) and BALB/c nude mice (sham, n=3; fs-THz, n=4; E~F) were exposed to the fs-THz beam for 1 hour. Skin samples were biopsied either at 1 and 24 hours after exposure of C57BL/6 mice or at 12 and 36 hours after exposure of BALB/C nude mice. Real-time quantitative polymerase chain reaction was used for gene expression survey: (A) substance P, (B) calcitonin gene-related peptide, (C, E) transient receptor potential vanilloid1 (TRPV1), (D, F) TRPV4. Results were expressed as

Comment [i]: Finally, in addition to the ion channels and transporters, we found that several plasma membrane receptors were differentially expressed in the THz-exposed cells. Arguably, the most intriguing finding was that many of these genes belong to the transient receptor potential (TRP) channel family. TRP channels are six-

Comment [i]: In this study we have shown that 2.52 THz radiation preferentially activates the expression of genes associated with the plasma membrane. Using the latest released microarray gene chips, we provide confirmation that human Jurkat cells exposed to THz radiation preferentially activate both plasma membrane genes and

mean±standard error of the mean. *$p < 0.05$, compared to the nonirradiated sham group.




A
EIF2 Signaling
Regulation of eIF4 and p70S6K Signaling
TGF-β Signaling
Neuregulin Signaling
Nur77 Signaling in T Lymphocytes
Axonal Guidance Signaling
PXR/RXR Activation
0.0
2.0
4.0
Enrichment (-log[P-value])
C
Tgfb1
Bmp2
Cd44
Krt6a
Lep
Serpine1
Sprr1b
Thbs1
Relative mRNA expression
SB431542
+ Activin
+ TGFβ
(NIH3T3)
B
Relative Tgfb1 expression
1 12 24 36 (h)
1 24 (h)
24 (h)
sham
THz
(C57BL/6J)
sham
THz
(BALB/c nude)
control
wound
(C57BL/6J)
D
Differentially expressed genes
Predicted transcription regulators
THBS1
SERPINB3
BMP2
CD44
SMAD4
SMAD3
NFKB1
AP1
TP63
CEBPA
CEBPB
TAF4
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CREB1
EGR1
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FOS
FOXL2
HIF1A
MYC
MYCN
JUN
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E
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+ Activin
+ TGFβ
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