

## Pneumatically Driven Laparoscope Holder Controlled by Head Movement

**THE NUMBER OF** laparoscopic surgeries and their applications have increased in recent years. In conventional laparoscopic surgery, a scopist has to hold the laparoscope and change its angle under the verbal instruction of the operating surgeon. The scopist needs a deep understanding of the surgical procedure and must have excellent dexterity. Camera shake may occur due to the fatigue of the scopist, which may cause the surgeon to get nauseous, especially in 3D vision. Therefore, a laparoscope holder is an important and effective advancement for laparoscopic surgery.

Laparoscope holders have been studied for many years, and some are commercially available. However, the operation methods such as voice control or switches in current laparoscopic holders are inferior in that they are not intuitive.

We have developed a laparoscope holder system, instead of a scopist holding the laparoscope, a robotic arm holds the camera, and the arm is positioned by the operator's head movements, as shown in Fig. 1. Robotic holders that have been previously developed use electrical motors for actuation. However, in this system, pneumatic actuators are used instead.

This is because pneumatic actuators have many safety advantages such as low heat generation, compressibility, the ability to control the maximum force by regulating the supply pressure, ease of releasing the acting force by discharging the compressed air in the actuator, and the ability to realize an arm that is both compact and lightweight (0.9Kg).

The robotic arm is controlled by the head movement measured using two gyroscopes attached to the operator's head and back. As shown in Fig. 1, the view angles of the laparoscope for up and down, left and right, and rotation synchronously follow the head rotations. The camera's zoom in and out synchronously follow the anteroposterior motions of the operator's head. We use gyroscopes in the proposed system.

The rotation speed during head movements is directly detected by the 3-axis gyroscope attached to the operator's head. The zoom in and out can be measured from the translation velocity of the head movement. The velocity can be theoretically obtained by integrating the data measured by an acceleration sensor attached to the operator's head.

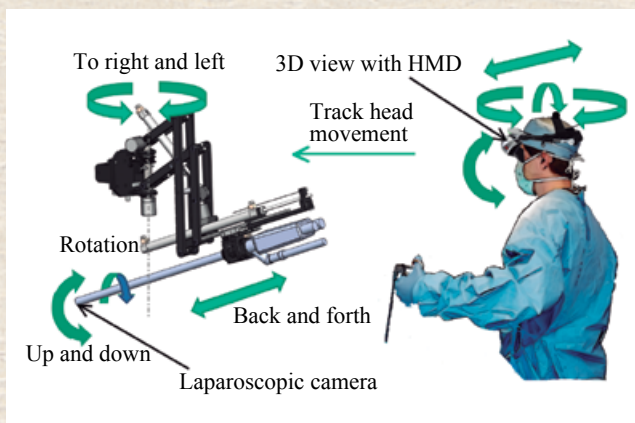
However, it is difficult to obtain an accurate velocity from the acceleration



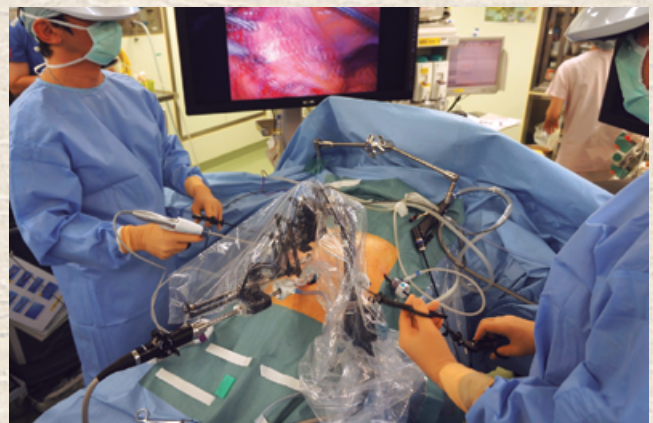
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sensor due to the errors caused by gravity compensation, drift of the zero point, and sensor noise. Therefore, we focused on the anteroposterior body movements of the operator. We estimated the translation movement of the head from the anteroposterior body movement based on a gyroscope attached to the operator's back. The estimated value is used as a control signal for the zooming movement of the robot.

The image of the laparoscope can be displayed to a monitor or on a head mount display (HMD). When the HMD is used as the monitor, the image is always kept in front of the operator's eyes, even when the operator turns his/her head. Therefore, using an HMD can provide highly intuitive operation and can avoid the need to consider the monitor layout. We confirmed the tracking accuracy of the system through experiments. Moreover, the effectiveness of the system was demonstrated through clinical trials as shown in Fig. 2. We are planning to commercialize the system in autumn this year.



**Fig. 1: Concept of the developed system**



**Fig. 2: Clinical trial**



## Discovery of a Novel Source of Dendritic Cells, the Control Tower of the Immune System

**A MAJOR REASON** people can stay healthy is the protection afforded by the body's immune system. This defense system is essential for performing a social life, and living out one's life. In the immune system, dendritic cells (DCs), distributed throughout the body as the most powerful antigen-presenting cells, activate immune cells upon viral infection, and maintain immune tolerance to self-antigen under steady-state conditions thereby preventing autoimmune diseases. DCs consist of two major subpopulations, i.e., conventional DCs (cDCs), which have excellent antigen-presenting capacity, and plasmacytoid DCs (pDCs), which have prominent type I interferon (IFN)-productivity.

The pDCs' activation and type I IFN production are critical for the initiation of anti-viral immune responses, whereas pDCs' activation in the absence of infection causes autoimmune diseases, such as systemic lupus erythematosus (SLE) and psoriasis vulgaris. Thus, the identification of DC progenitors that give rise strictly to cDCs or pDCs, but not to other hematopoietic cells (Fig. 1), could be important in medical applications for treating viral infections and autoimmune diseases.

Our research group, led by Dr. Nobuyuki Onai, has recently discovered

the DC progenitors, a novel source of dendritic cells (DCs). In 2007, in collaboration with a research group in Switzerland, we identified progenitor cells committed to the DC lineage for the first time. However, these progenitors gave rise to many more cDCs than pDCs, implying that there must be another unidentified type of DC progenitor that serves as a major source of pDCs. Under the background, we focused on finding progenitor cells that serve as a major source of pDCs and that were closely related to the previously identified ones. After a long search, we successfully identified a DC progenitor with prominent pDC differentiation potential. Importantly, each of these DC progenitors can give rise to 500~1,000 DCs. The number of pDCs generated from each of the new DC progenitor cells is several times higher than that from the previously reported DC progenitor, and the new DC progenitor highly expresses E2-2, a basic helix-loop-helix transcription factor essential for pDC development and survival. Since both the previous and newly identified DC progenitors strictly give rise to DCs, and the former expresses M-CSF receptor (MCSFR) whereas the latter does not, we designate them by the term, M-CSFR<sup>+</sup> com-



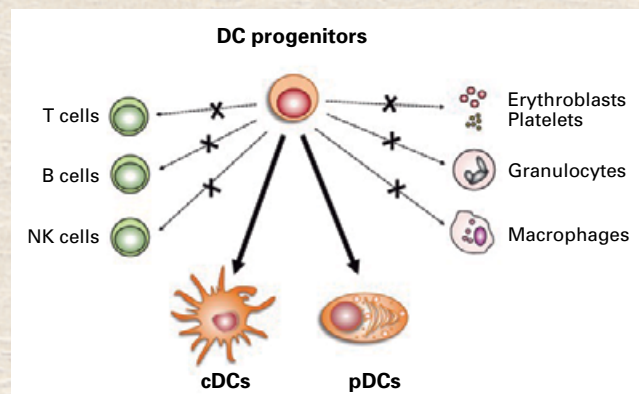
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mon DC progenitors (CDPs) and M-CSFR<sup>-</sup> CDPs, respectively (Fig. 2). What then is the relationship between the previous and this distinct DC progenitors? We propose that the former might produce the latter by stimulating with M-CSF or thrombopoietin (TPO). In addition, we further found that the CDPs appear to be directly derived from lymphoid-primed multi-potent progenitors (LMPPs), the end stage of MPP.

As DCs have recently received much attention as a potential target for vaccine development against infectious diseases and cancer, our findings, the identification of DC progenitors that produce 500-1,000 DCs and no other hematopoietic cells, may provide insight into DC differentiation pathways and may also be valuable in the development of therapeutic applications for infectious diseases, cancers, and autoimmune diseases.

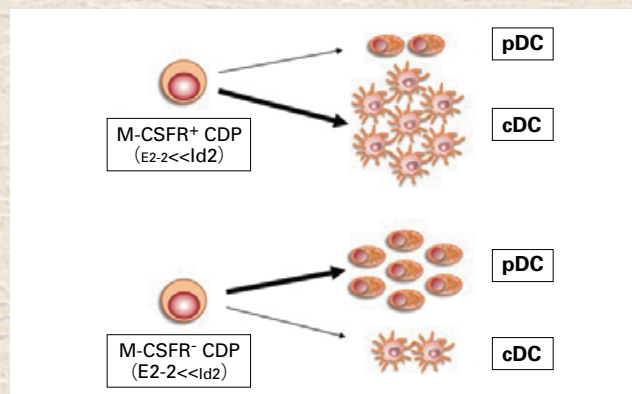
### References

1. Onai, N. et al., A clonogenic progenitor with prominent plasmacytoid dendritic cell developmental potential. *Immunity* 38, 943-57 (2013)
2. Shortman, K., and Sathe Priyanka. Another heritage for plasmacytoid dendritic cells. *Immunity* 38, 845-46 (2013)



**Fig. 1: Definition of DC progenitors**

DC progenitors give rise strictly to cDCs or pDCs, but not to other hematopoietic cells.



**Fig. 2: M-CSFR<sup>+</sup> CDP and M-CSFR<sup>-</sup> CDP**

M-CSFR<sup>+</sup> CDPs give rise to many more cDCs than pDCs, whereas M-CSFR<sup>-</sup> CDPs give rise to many more pDCs than cDCs.



## Rapid Attachment of Artificial Materials to Bone Surface

**WE HAVE DEVELOPED** the novel technology for rapid biological attachment of artificial devices to the surface of bone substances. Presently, biocompatible materials as titanium and hydroxyapatite enables surgeons to attach devices implanted to bones through osseointegration (direct attachment of materials to bone tissue) and are utilized in many clinical applications including artificial joints and artificial tooth roots.

In the use of such materials, however, significant invasions to bones are required at device implantation since the bone forming cells derived from bone marrow are necessary for generation of bone tissue on the materials. In the cases of placement of devices to the bone surface, the scenario is quite different. Prior to the placement, surgeons have to peel off the membranes covering the bone surface. During this maneuver, the bone forming cells are severely damaged and no such cells could be recruited around the devices; hence realization of biological attachment to bone surface is a very difficult task.

Albeit the difficulty in osseointegration technology onto the bone surface, it will enable us to realize quite number of innovations in clinical devices. One of the great possibilities lies in the field of orthodontics. Actually, various kinds of devices have been created in the orthodontic treatment, with the use of



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such devices orthodontist applied particular mechanical load to the tooth and generate the desired tooth movement. If such devices are fixed to the bone, their efficacy will increase significantly. Recent progress in dental implants already demonstrated such possibility, however, such implants inevitably accompanied with considerable invasion. Hence we investigated the technology for rapid attachment of artificial materials to bone surface.

We had to improve the surface characteristics to realize the direct attachment of materials to bone. Either titanium or hydroxyapatite, conventionally utilized materials for osseointegration, would induce fibrous soft tissue around the materials due to the absence of bone forming cells. We therefore adopted a brand new nanocomposite material, hydroxyapatite/collagen (HAp/Col) which was developed by researchers of National Institute of Materials Science (NIMS) and TMDU. This composite has a unique function of bioabsorbability; commonly known bioabsorbable materials are spontaneously degraded in the in vivo milieu and resorbed whereas



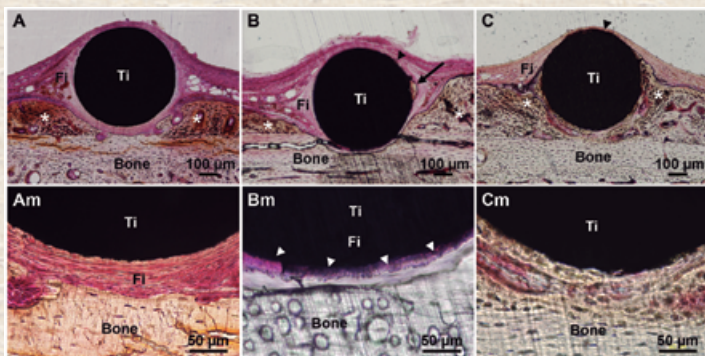
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HAp/Col is ingested through phagocytic processing of cells. The enhanced activity of bone forming cells around HAp/Col had been proved in clinical trials and now the HAp/Col sponges are commercially available as the bone filling materials. These two characteristics, phagocytic processability and activation ability for bone forming cells are favorably employed for our intended usage of materials.

The technology developed in this study was the dip coating of HAp/Col to the surface of titanium. The efficacy of the technology was confirmed in the animal model in which coated titanium rods were placed under the periosteal membrane of rat's calvaria. The controls for comparison were bare titanium rods and conventional HAp coated rods. Dr Masayuki Kikuchi of NIMS, the inventor of HAp/Col, donated us the materials with kind expertise, and the experiments were performed by PhD candidate Masayoshi Uezono. Typical microscopic observation is shown in the figure. Bare titanium rod (A) and HAp coated titanium rod (B) was totally capsulated by soft fibrous tissues and no attachment to bone was realized. On the other hand, the HAp/Col coated rod (C) attached to bone.

Thus developed HAp/Col coating technology would be applied to various fields of dentistry and surgery. We are now promoting the joint investigation with a dental device company for the experiment with large animals, and expecting the device will be in clinical use in near future.



**Fig. 1:** Bare titanium rod (A) and HAp coated titanium rod (B) was capsulated by soft fibrous tissues whereas HAp/Col coated titanium rod (C) attached directly to bone tissue.