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Pulpal Regeneration Following Allogenic Tooth Transplantation into Mouse Maxilla

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ABSTRACT

Autogenic tooth transplantation is now a common procedure in dentistry for replacing a missing tooth. However, there are many difficulties in clinical application of allogenic tooth transplantation because of immunological rejection. This study aims to clarify pulpal regeneration following allogenic tooth transplantation into the mouse maxilla by immunohistochemistry for 5-bromo-2′-deoxyuridine (BrdU) and nestin, and by the histochemistry for tartrate-resistant acid phosphatase (TRAP). The upper right first molar (M1) of 2-week-old mice was extracted and allografted in the original socket in both the littermate and non-littermate after the extraction of M1. Tooth transplantation weakened the nestin-positive reactions in the pulp tissue that had shown immunoreactivity for nestin before operation. On postoperative Days 5–7, tertiary dentin formation commenced next to the preexisting dentin where nestin-positive odontoblast-like cells were arranged in all cases of the littermate group until Day 14, except for one case showing immunological rejection in the pulp chamber. In the non-littermate group, bone-like tissue formation occurred in the pulp chamber in addition to tertiary dentin formation until Day 14. The rate of tertiary dentin was 38%, and the rate of the mixed form of dentin and bone-like tissue formation was 23% (the remainder was immunological rejection). Interestingly, the periodontal tissue recovered even in the case of immunological rejection in which the pulp chamber was replaced by sparse connective tissue. These results suggest that the selection of littermate or non-littermate is decisive for the survival of odontoblast-lineage cells and that the immunological rejection does not influence the periodontal regeneration. Anat Rec, 292:570–579, 2009.

Key words: allo-graft; bone development; dental pulp; tooth transplantation; mouse (Cdlj:CD;ICR)

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Autogenic tooth transplantation is now a common procedure in dentistry for replacing a missing tooth in patients in whom implants and other prosthetic replacements are contraindicated for various reasons. Tooth transplantation offers one of the fastest and most economically feasible means of replacing a missing tooth (Kallu et al., 2005). The success rate of autogenic tooth transplantation varies from 80% to 96% (Slagsvold and Bjercke, 1974; Kristerson, 1985; Andreasen et al., 1990a,b; Cohen et al., 1995; Lundberg and Isaksson, 1996; Mejàre et al., 2004; Kim et al., 2005), and this rate is influenced by a number of preoperative and postoperative factors such as the age of the patient, root developmental stage, type of tooth transplanted, periodontal ligament and pulp tissue vitality, extra-alveolar time and storage medium of the donor tooth, damage of Hertwig's epithelial root sheath during extraction, and characteristics of the recipient site (Andreasen et al., 2007). On the other hand, previous publications on allografting teeth suggest a low success rate, which is probably related to histocompatibility (Andreasen et al., 1990a,c). As the dental pulp and the periodontal ligament are two major sources of alloantigens in the tooth, pulpal necrosis of allografts is inevitable due to histocompatibility differences (Riviere, 1981). The survival time for allografts occasionally continues for many years despite a progressing replacement resorption (ankylosis) inevitably present (Schwartz et al., 1987). The major complications of tooth transplantation are external inflammatory root resorption and ankylosis (Andreasen et al., 2007). Inflammatory resorption is caused by the irritation derived from pulp necrosis and subsequent infection (Heithersay, 1999; Trope, 2002), whereas ankylosis is caused by damage to the periodontal ligament during the surgical procedure (Andreasen, 1981). However, pulpal responses to tooth transplantation are unclear except for clinical diagnosis such as radiographical analysis and clinical sign.

Tooth replantation is also a common procedure in dentistry for the treatment of the complete luxation of teeth. In successful cases, pulpal regeneration, reinnervation, and revascularization have been shown to occur in humans (Andreasen et al., 1995) and in experimental animal studies (Kvinnsland et al., 1991; Byers et al., 1992; Rungvechvuttivittaya et al., 1998; Shimizu et al., 2000; Ohshima et al., 2001; Nakakura-Ohshima et al, 2003; Tsukamoto-Tanaka et al., 2006; Hasegawa et al., 2007). Pulpal responses to tooth replantation can be divided into at least two types: tertiary dentin and bone-tissue formation in the regenerated pulp tissue (Kvinnsland et al., 1991; Byers et al., 1992; Rungvechvuttivittaya et al., 1998; Shimizu et al., 2000; Ohshima et al., 2001; Tsukamoto-Tanaka et al., 2006; Hasegawa et al., 2007; Zhao et al., 2007). Our recent experimental study using autogenic tooth transplantation supports that odontoblast- and osteoblast-lineage cells reside in the dental pulp (Ogawa et al., 2006). In the case of tooth replantation, furthermore, the appearance of osteoclast-lineage cells may be associated with the induction of bone tissue in dental pulp. Once these cells appear at the pulp-dentin border, bone matrix deposition can be induced, even beneath the preexisting dentin (Tsukamoto-Tanaka et al., 2006). Thus, the dental pulp may have multilineage differentiation capability. Recent study suggests that the lack of proper oxygenated medium is decisive for the survival of odontoblast-lineage cells and that the occlusal force during and/or after the operation make the fate of these cells worse (Hasegawa et al., 2007).

With respect to the clinical use of tooth transplantation, there is probably no place for allografting of teeth today due to the possibility of disease transmission and the higher success rate of autotransplants (Cohen et al., 1995). However, the cases that are susceptible to tooth transplantation would be considerably increased in range, if allogenic transplants become a common procedure in dentistry. For example, allogenic tooth transplantation becomes an alternative treatment for replacing a missing tooth, when a suitable donor tooth is not available in the case of autogenic transplants. Recently, we established an experimental model for allogenic tooth transplantation using mouse molars (Kim et al., 2006). In this preliminary study, we failed to lead pulp regeneration after allografts into the maxilla, because the age of animals (4-week-old mice) was not suitable for blood supply into the pulp chamber via the apical foramen. We modified this model to realize a successful experimental model for allogenic tooth transplantation where pulpal regeneration, reinnervation, and revascularization occurred by using younger animals (2-week-old mice) than before. If we can establish the successful experimental animal model using mice for allogenic tooth transplantation into the maxilla, this kind of animal model could be available for the clarification of genetic mechanisms under pathological conditions using various transgenic mice. Thus, this study aims to clarify pulpal regeneration following allogenic tooth transplantation into the mouse maxilla by immunohistochemistry for 5-bromo-2′-deoxyuridine (BrdU) as a cell proliferation assay and nestin as an odontoblastic marker (Terling et al., 1995; About et al., 2000; Ogawa et al., 2006; Hasegawa et al., 2007), and by the histochemistry for tartrate-resistant acid phosphatase (TRAP) as a marker for osteoclast-lineage cells (Bonucci and Nanci, 2001).

MATERIALS AND METHODS

Operation for Tooth Transplantation

All experiments were reviewed by the Committee on the Guidelines for Animal Experimentation of Niigata University and performed according to the recommendations or under the conditions proposed by the Review Committee. The upper right first molar (M1) of Crlj:CD1 (ICR) mice (2 weeks old) was extracted after making the mucus membrane flap due to the presence of oral mucosa covering an unerupted tooth, under deep anesthesia by an intraperitoneal injection of chloral hydrate (the maximum dose of 350 mg/kg). The tooth extraction was performed with a pair of modified dental forceps and then the extracted tooth was allografted in the original socket in either the littermate or non-littermate after the extraction of M1. The flap was replaced in the original position after the completion of allograft without any further treatments such as suturing. Prolonged inflammatory reactions never occurred after operation, resulting in the success rate being 100%, although immunological rejections occasionally occurred in the dental pulp of transplanted teeth (Table 1). The operation did not influence the feeding of animals or the eruption of teeth. The untreated upper left M1 of the same animal was used as a control.

TABLE 1. Healing patterns in the dental pulp at 14 days after allogenic tooth transplantation in the littermates and non-littermates in this study

	Rejection	Inflammation	Dentin & bone	Bone	Dentin
Littermates	8% (1/13)	0% (0/13)	0% (0/13)	0% (0/13)	92% (12/13)
Non-littermates	38% (5/13)	0% (0/13)	23% (3/13)	0% (0/13)	38% (5/13)

The rate of tertiary dentin formation in the transplant model using the littermates in this study is significantly higher in comparison with the replant model (Table 2).

Tissue Preparation

Materials were collected from groups of 3–12 animals at intervals of 1, 3, 5, 7, and 14 days in the littermates (the total number was 33) and 10–13 animals at intervals of 7 and 14 days in non-littermates (the total number was 23) after tooth transplantation. At each stage, the animals were administered with an intraperitoneal injection of BrdU (150 mg/kg) 2 hr before the fixation and transcardially perfused with physiological saline followed with 4% paraformaldehyde in 0.1 M phosphate buffer (pH 7.4) under deep anesthesia by an intraperitoneal injection of chloral hydrate (350 mg/kg). The maxillae were removed *en bloc* and immersed in the same fixative for an additional 12 hr. Following decalcification in 10% ethylenediamine tetra-acetic acid disodium salt (EDTA-2Na) solution for 2 weeks at 4°C, the specimens were embedded in paraffin and sagittal sections of teeth were cut at 5 μm. The paraffin sections were mounted on Matsunami adhesive silane (MAS)-coated glass slides (Matsunami Glass, Osaka, Japan) and stained with hematoxylin and eosin (H&E).

Immunohistochemical Analysis

For the immunoperoxidase procedure, sections were processed with the Calbiochem BrdU Immunohistochemistry System (EMD Biosciences, Darmstadt, Germany) and Nichirei Histofine Simple Stain Mouse MAX-PO (Nichirei Biosciences, Tokyo, Japan) with a mouse anti-nestin monoclonal antibody diluted 1:50 (Chemicon International, Temecula, CA). The sections were counter stained with hematoxylin or 0.05% methylene blue. The brown color in the BrdU-labeled cells was transferred into a red color and graphically emphasized by using graphic software (Adobe Photoshop CS2 for Windows; Adobe Systems Incorporated, San Jose, CA). Immunohistochemical controls were performed by (1) replacing the primary antibodies with non-immune serum or PBS and (2) omitting the streptavidinperoxidase or the MAX-PO solution. These immunostained sections contained no specific immunoreaction.

Histochemical Analysis

For the histochemical demonstration of TRAP activity, the azo-dye method was utilized with slight modification (Tsukamoto-Tanaka et al., 2006). The paraffin sections were incubated for 15 min at room temperature in a medium comprising 0.01% naphthol AS-BI phosphatase (Na salt; Sigma Chemical, St. Louis, MO), 0.06% fast red violet LB salt (Sigma Chemical) and 50 mM L-(+)-tartaric acid in 0.2 M acetate buffer (pH 5.3). The sections were counter-stained with 0.5% methyl green.

Quantitative Analysis of Cell Proliferation

The number of BrdU-positive cells in the coronal and root pulp areas was calculated in the samples at 3–14 days after tooth transplantation in the littermate group. Quantitative analysis was performed on three areas in the coronal pulp and one to two areas in the root pulp for each sample. The data were obtained from the samples of 16 animals (the number in each group was one to three; the final number of areas was 73), the grid (304×243 μm^2) was selected at random in each area (coronal and root pulp). All data were represented as the means and standard deviations (SD) of each group. Furthermore, the number of cells in the coronal and root pulp among different times after transplantation was compared using Bonferroni's test (one-way analysis of variance; ANOVA) by using statistical software (SPSS 14.0J for Windows; SPSS Japan, Tokyo, Japan).

RESULTS

Histological Changes in the Dental Pulp of Transplanted Teeth in the Littermate Group

In the control group, nestin-immunoreactivity was exclusively expre-ssed in the coronal and root odontoblasts, and the other types of cells lacked positive reactions in the dental pulp (Fig. 1a). On postoperative Days 1–3, the pulp chamber was mainly occupied by inflammatory lesions including numerous neutrophils, fibrin networks, and a hemorrhage (Fig. 1b–d), and nestin-positive odontoblasts disappeared in the pulp chamber by Day 3 (data not shown). The odontoblast-like cells came to be arranged along the pulp-dentin border in the coronal and root pulp and expressed nestin-positive reactions on Day 5 (Fig. 2a,c), although the vast majority of coronal pulpal cells were devoid of positive immunoreactions for nestin. Nestin-positive odontoblast-like cells were arranged along the pulp-dentin border throughout the dental pulp on Day 7 (data not shown). The tertiary dentin (92% [12/13]; Table 1) was deposited in the pulp tissue by Day 14 (Fig. 3a,b), although the cells were occasionally embedded in the matrix which was determined as dentin because of the presence of nestin-positive reactions in the cells surrounding the matrix (Fig. 3c,d). The distinction between dentin and bone-like tissue was determined by the existence of nestin-positive cells in the case of dentin (Fig. 3b,d) and the cell inclusion without nestin-positive reactions in the case of bone-like tissue (Fig. 4b), because osteoblast-like cells showed no intense nestin-immunoreactivity (Ogawa et al., 2006). The immunological rejection rarely occurred in the dental pulp (the rate was 8% [1/13]; Table 1).

The pulp tissue in the control group contained no TRAP-positive reaction, whereas intense TRAP-positive reactions were observed inside the bone marrow and

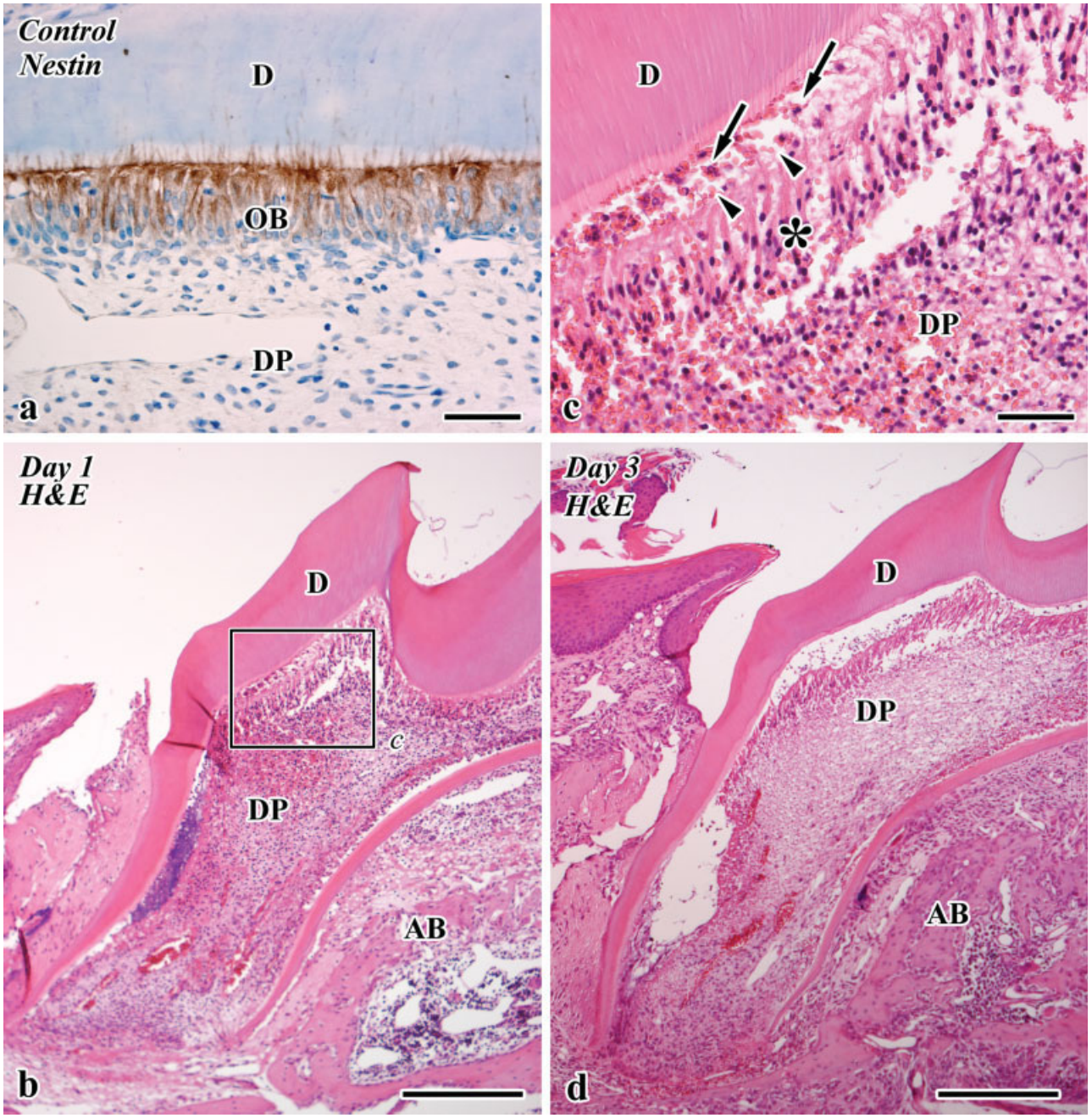

Fig. 1. H&E staining (b–d) and nestin-immunoreactivity (a) in the sections of the mesial portion of control (a) and transplanted teeth at 1 (b,c) and 3 (d) days after operation in the littermates. (**a**) Odontoblasts (OB) are positive for nestin-immunoreactivity, and the other types of cells lack positive reactions in the dental pulp (DP). (**b**) The pulp chamber is mainly occupied by inflammatory lesions including numerous neutrophils, fibrin networks, and a hemorrhage. (**c**) Higher magnification of the boxed area labeled by *c* in b. Neutrophils (arrows) and red blood cells (arrowheads) are observed in the degenerating odontoblast layer (*). (**d**) Coronal pulp still contains numerous inflammatory cells. AB, alveolar bone; D, dentin. Scale bars = 250 μm in b,d, 50 μm in a,c.

around the bone tissue (data not shown). Tooth replantation did not influence TRAP-positive reactions in the pulp chamber, although TRAP-positive reactions increased in intensity in the periodontal tissue and were recognized on the surface of root dentin until Day 5 (Fig. 2b). TRAP-positive cells occasionally appeared in the pulp chamber in areas in which odontoblast-like cells were not discernible (Fig. 2d).

Histological Changes in the Transplanted Dental Pulp in the Non-littermate Group

The morphological features on Day 7 in the transplanted dental pulp of the non-littermate group were basically the same as those in the littermate group (data not shown). On Day 14, two healing patterns, i.e., the tertiary dentin (the rate was 38% [5/13]; Fig. 4c, Table

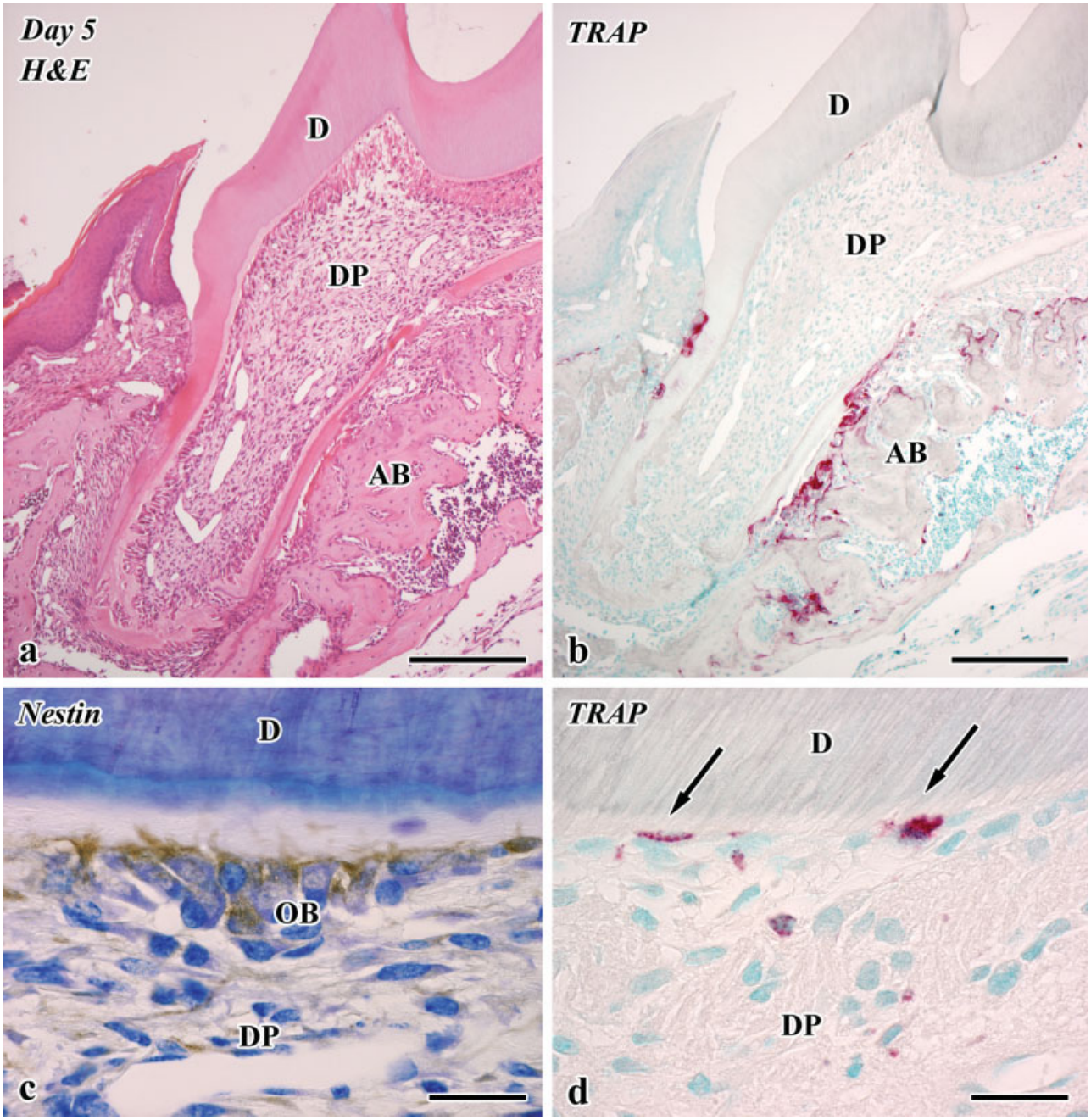

Fig. 2. H&E staining (a), nestin-immunoreactivity (c), and TRAP-reactions (b,d) in the sections of the mesial portion of transplanted teeth at 5 days after operation in the littermate. (**a**) Inflammatory lesion almost ceases and blood supply is recovered in the dental pulp (DP). (**b**) Pulp chamber contains no TRAP-positive reaction, whereas TRAP-positive reactions are increased in intensity in the periodontal tissue and recognized on the surface of root dentin. (**c**) The odontoblast-like cells (OB) come to be arranged along the pulp-dentin border in the coronal and root pulp and express nestin-positive reactions. (**d**) TRAP-positive cells (arrows) occasionally appear in the pulp chamber in areas in which odontoblast-like cells are not discernible. AB, alveolar bone; D, dentin. Scale bars = 250 μm in a,b, 25 μm in c,d.

1) and the mixed features of tertiary dentin and bone-like tissue (the rate was 23% [3/13]; Fig. 4a,b, Table 1), occurred in the pulp tissue, in addition to the case of immunological rejection in the pulp chamber (the rate was 38% [5/13]; Fig. 4d,e, Table 1), although the immunological rejection was not recognizable in the pulp chamber on Day 7. The tertiary dentin formation was recognized beneath the preexisting dentin (Fig. 4e), and the periodontal tissue recovered even in the case of immunological rejection in which the pulp chamber was replaced by sparse connective tissue (Fig. 4d). The rate of tertiary dentin formation was significantly lower in

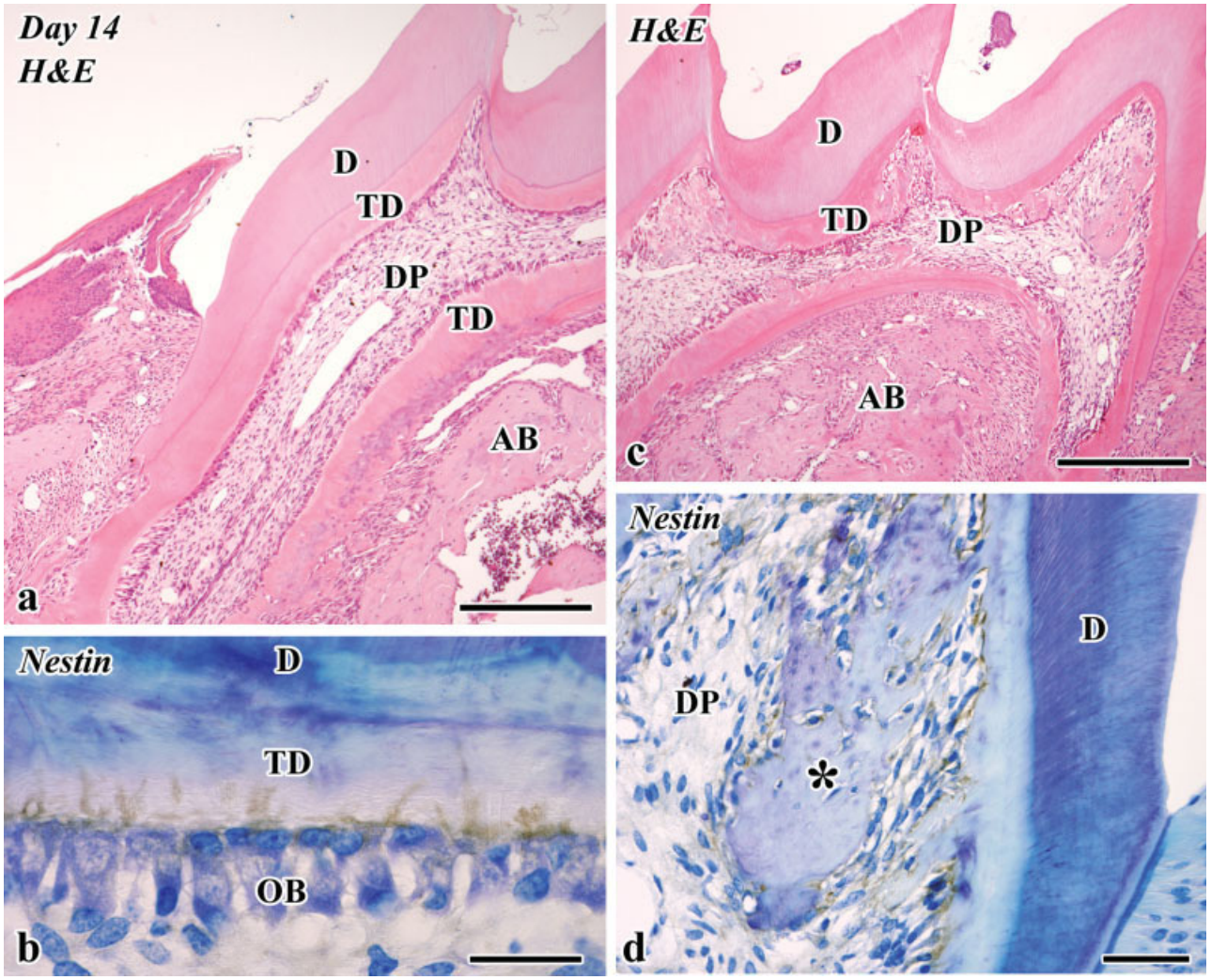

Fig. 3. H&E staining (a,c) and nestin-immunoreactivity (b,d) in the sections of transplanted teeth at 14 days after operation in the littermates. (**a**) Clear tertiary dentin is deposited in the periphery of dental pulp (DP). (**b**) Nestin-positive odontoblast-like cells (OB) are arranged along the pulp-dentin border throughout the dental pulp. (**c**) The matrix, which morphologically looks like bone-like tissue, occasionally occurs in the pulp tissue. (**d**) The matrix (*), where the cells are embedded, is determined as dentin because of the presence of nestin-positive reactions in the surrounding cells. AB, alveolar bone; D, dentin; TD, tertiary dentin. Scale bars = 250 μm in a,c, 50 μm in d, 25 μm in b.

the non-littermate group (the rate was 38%; Table 1) than that in the littermate group (the rate was 92%; Table 1). TRAP-positive cells occasionally appeared in the pulp-dentin border and extended their cellular processes into the dentinal tubules in cases in which tertiary dentin was not deposited (Fig. 4f).

Cell Proliferation Assay by BrdU Labeling

In the control, the dental pulp contained few BrdU-positive cells (data not shown). No BrdU-positive cells were recognized in the pulp chamber on Day 1 (data not shown). They were significantly increased in number in the coronal pulp on Day 5, and subsequently they were significantly decreased in number by Day 14 (Figs. 5 and 6).

DISCUSSION

An experimental animal model using mice for allogenic tooth transplantation has been established in the present study. This article is the first report on the animal experimental model using mice except for one preliminary paper (Kim et al., 2006), as previous studies on allogenic tooth transplantation into the jaw were performed via experimental models using rabbits, dogs, and monkeys (Mirzabagi, 1978; Riviere, 1981; Runyon et al., 1986). These previous reports did not focus on the pulpal regeneration process after tooth transplantation. In contrast, numerous experimental animal studies on tooth replantation focused on the pulpal regeneration after operation (Kvinnsland et al., 1991; Byers et al., 1992; Rungvechvuttivittaya et al., 1998; Shimizu et al., 2000;

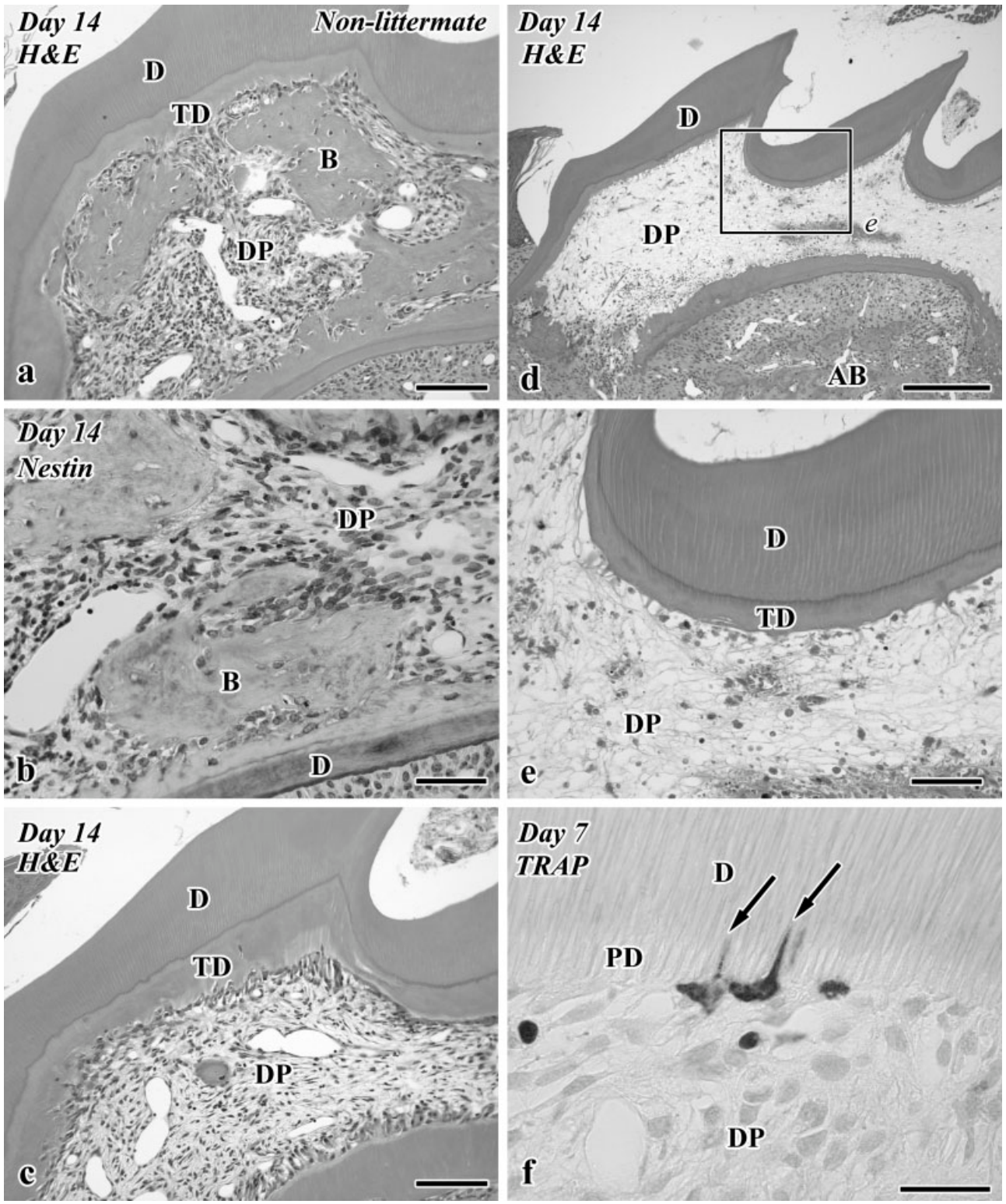

Fig. 4. H&E staining (a,c–e), nestin-immunoreactivity (b), and TRAP-reactions (f) in the sections of the mesial portion of transplanted teeth at 7 (f) and 14 (a–e) days after operation in the non-littermates. (**a**) The mixed features of tertiary dentin (TD) and bone-like tissue (B) occur in the dental pulp (DP). (**b**) The bone-like tissue is devoid of nestin-positive reactions in the surrounding cells. (**c**) Tertiary dentin is observed in the periphery of pulp tissue. (**d**) The periodontal tissue recovers even in the case of immunological rejection in which the pulp chamber is replaced by sparse connective tissue. (**e**) Higher magnification of the boxed area labeled by *e* in d. Tertiary dentin formation is recognized beneath the preexisting dentin (D). (**f**) TRAP-positive cells occasionally appear in the pulp-dentin border and extend their cellular processes into the dentinal tubules (arrows) in the case in which tertiary dentin is not deposited. AB, alveolar bone. Scale bars = 250 μm in d, 100 μm in a,c, 50 μm in b,e, 25 μm in f.

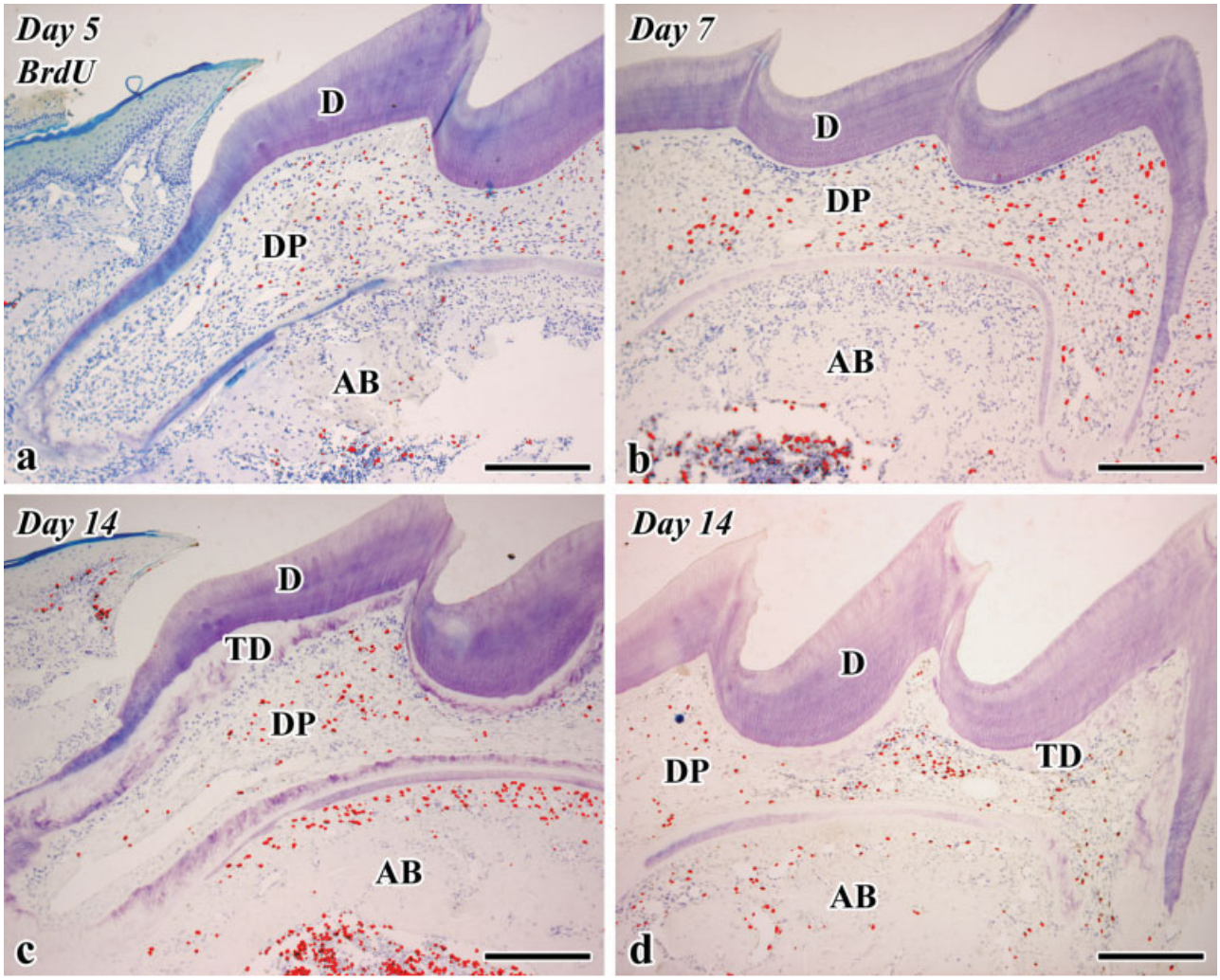

Fig. 5. BrdU-labeled sections of the transplanted teeth at 5 (a), 7 (b), and 14 (c,d) days after operation in the littermates. BrdU-positive reactions are colored red. **a–d**: The number of BrdU-positive cells is very large in the pulp chamber on Days 5–7 (a,b), and subsequently they are decreased in number on Day 14 (c,d). AB, alveolar bone; D, dentin; DP, dental pulp; TD, tertiary dentin. Scale bars = 250 μm.

Ohshima et al., 2001; Nakakura-Ohshima et al., 2003; Tsukamoto-Tanaka et al., 2006; Hasegawa et al., 2007). Among them, a recent study succeeded in establishing an experimental animal model using mice for tooth replantation (Hasegawa et al., 2007). The pulpal healing process after allogenic tooth transplantation in this study is similar to that in the previous experimental model for tooth replantation (Hasegawa et al., 2007), suggesting that pulpal responses to tooth replantation can be divided into at least two types: tertiary dentin and bone-like tissue formation in the regenerated pulp tissue (Table 2). Furthermore, cell proliferative activity in the dental pulp of transplanted teeth is almost the same as that of the replanted teeth: dental pulp cells most actively proliferate on Day 5 after operation, and their proliferative activity weakens by Day 14. However, the detailed healing patterns differed between these different models. The most striking difference is the occurrence of immunological rejection in the allografts (the rate was 38%), although the rate of immunological rejection was low in the case of the use of littermate (the rate was 8%). Conversely, the rate of tertiary dentin formation in the transplant model (92%) using the littermate in this study was significantly higher in comparison with the replant model (43%; the rate reaches 60%, if the counterpart tooth of the replanted tooth is extracted, suggesting that occlusal force during and/or after operation worsens the fate of odontoblast lineage cells: Table 2; Hasegawa et al., 2007). Furthermore, there are prolonged inflammatory reactions via oral bacterial infections to prevent the pulpal regeneration in the replants (20–21%: Table 2; Hasegawa et al., 2007). The findings may be attributed to the differences in the age of the animals between these different models: 2-week-old mice are used for the transplants and 3-week-old mice for the replants. As the apical foramens gradu-

ally become reduced in size according to the progress of root formation, younger animals are more favorably predisposed to the revascularization and reinnervation into the pulp chamber after tooth transplantation. It has been reported that the donor tooth should ideally present one third to three quarters of root formation to allow normal root development (apexogenesis) and revascularization of the human pulp tissue (Mejàre et al., 2004; Kallu et al., 2005; Kim et al., 2005). Furthermore, the oral mucosa covering the transplant after operation may have the advantage of preventing bacterial invasion, as M1 has not erupted into the oral cavity at 2 weeks after birth, in addition to the fact that the mice at this stage are still suckling to provide a more sterile oral environment compared with the older mice that have already weaned. Thus, the recovery of vasculature in the pulp tissue in the early stage and the prevention of infection may accelerate the differentiation of odontoblast-like cells in the transplants in this study. From a clinical point of view, the unerupted third molar, wisdom tooth, in the human teenager could be a candidate for the donor of allograft.

The distinction between dentin and bone-like tissue was determined by both the immunoreactivity for nestin and the existence of cell inclusion in the matrix in this study. However, the definition of bone-like tissue in this study may be vague, because of the occurrence of the cell-embedded matrix being positive for nestin-immunoreactivity and devoid of tubular structures. This situation is the same as the case of an experimental model for tooth replantation using mice (Hasegawa et al., 2007). On the other hand, the appearance of osteoclast-lineage cells is always associated with the induction of bone-like tissue formation in dental pulp following tooth replantation using rats in the previous study (Tsukamoto-Tanaka et al., 2006), suggesting that TRAP reactions are available for the distinction of bone-like tissue in the rat models. However, the appearance of TRAP-positive cells was rare in the present and previous studies using mice (Hasegawa et al., 2007), despite the close relationship between the appearance of intense TRAP-positive cells and the induction of bone-like tissue formation as demonstrated in our recent autogenic tooth transplantation using mice (Ogawa et al., 2006). These results indicate that the microenvironment after tooth injury differs among different experimental models: severe damage may induce the typical bone tissue associated with TRAP-positive cells.

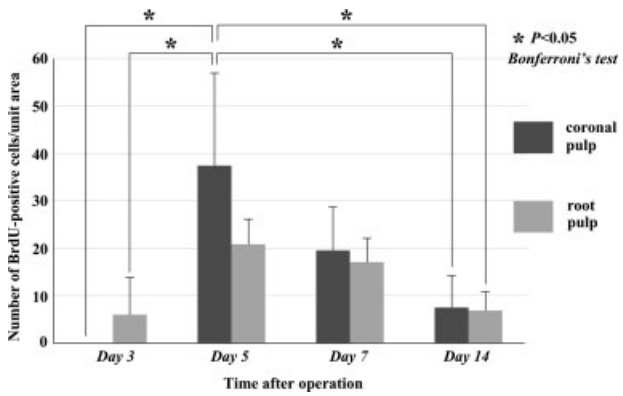

Fig. 6. Quantitative analysis of cell proliferation in the dental pulp of transplanted teeth at 3, 5, 7, and 14 days after operation in the littermates. The number of BrdU-positive cells is counted in the unit area (304 $\times$ 243 μm^2) in both the coronal and root pulp. BrdU-positive cells are significantly increased in number in the coronal pulp on Day 5, and subsequently they are significantly decreased in number on Day 14.

It is noteworthy that no immunological rejection occurred in the pulp chamber in any experimental sample on Day 7, and that the tertiary dentin was formed beneath the preexisting dentin even in the case of immunological rejection in which the pulp chamber was replaced by sparse connective tissue on Day 14. The results indicate that the donor cells first differentiated into odontoblast-like cells and subsequently these cells suffered death by the attack of immune cells (cytotoxic T lymphocytes), resulting in the sparse connective tissue replacing the pulp tissue. Interestingly, the periodontal tissue recovers even in the case of immunological rejection. Our previous study using *LacZ* transgenic ROSA26 mice clearly demonstrated that donor periodontal mesenchymal cells are replaced by host cells and that periodontal tissue can regenerate after allogenic tooth transplantation (Kim et al., 2006). Thus, even after an immunological rejection occurs to delete the donor cells, the periodontal tissue could regenerate, whereas the pulp tissue could transform into the sparse connective tissue. Further studies are required to clarify the fate of donor cells by using the allograft transplantation experiments using green fluorescent protein (GFP) or ROSA26 reporter mice and the long-term fate of the transplants in this experimental model. Exact knowledge of the biological properties of the pulp and periodontal tissues, especially each regenerative capability and the mechanisms of the pulp and periodontal tissues regeneration following allogenic tooth transplantation, would provide useful information for future regenerative treatment of the pulp and periodontal tissues.

TABLE 2. Healing patterns in the dental pulp at 14 days after tooth replantation with/without the extraction of counterpart tooth on the basis of the results in the previous study (Hasegawa et al., 2007)

	Rejection	Inflammation	Dentin & bone	Bone	Dentin
Without extraction	0% (0/14)	21% (3/14)	29% (4/14)	7% (1/14)	43% (6/14)
With extraction	0% (0/15)	20% (3/15)	20% (3/15)	0% (0/15)	60% (9/15)

The rate of tertiary dentin formation in the replant model is significantly lower in comparison with the transplant model using the littermates (Table 1) in this study.

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