Donor-derived oral squamous cell carcinoma
After allogeneic bone marrow transplantation

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Running title: Donor-derived epithelial cancer after BMT

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Abstract

In animal models, tissue stem cells were proposed to exhibit an unexpected level of plasticity, although issues on cell fusions have lead to some controversies. Only transplantation experiments using genetically distinct recipients and donors can unequivocally demonstrate these changes in cell fate. We have analyzed oral squamous cell carcinomas arising in 8 patients long term survivors of allogeneic bone marrow transplantation, where chronic graft-versus-host disease greatly favors development of squamous cell carcinomas, possibly as a consequence of lichenoid mucosal inflammation. Using two independent methods, i) combined immunostaining and fluorescent in situ hybridization (FISH) analysis for X and Y chromosomes sequences in sex-mismatched grafts, and ii) comparison of micro-satellite typing of laser-microdissected tumor, donor, and recipient cells, in all tumors, we demonstrated that 4 of these 8 epithelial tumors actually arose from the engrafted allogeneic bone marrow. Thus, donor-derived bone marrow cells, whether hematopoietic or mesenchymal, recruited to sites of chronic mucosal inflammation yielded epithelial tumors. Our observations therefore demonstrate that marrow cells in human have a major role in epithelial cancer formation following allogeneic transplantation.
Introduction

Squamous cell carcinomas (SCC) are rare, though well recognized, complications of bone marrow transplantation (BMT) \(^1\)\(^2\). Studies in bone marrow transplant recipients have demonstrated the donor origin of hepatocytes, in rodents and later in humans \(^3\), and of hepatic oval cells, skeletal muscle cells and astrocytes in rodents (reviewed in reference \(^3\)). Experimental studies even demonstrated the multi-organ, multi-lineage engraftment by a single bone marrow-derived stem cell of donor origin, underlining the ability of bone marrow stem cells for transdifferentiation into other cell types than blood cells \(^4\). Yet, the possibility of cell fusion has raised serious concerns and complicated the analysis of developmental plasticity of bone marrow–derived cells \(^5\)\(^6\), yielding considerable controversies. Recently, mesenchymal stem cells have been characterized in human. These cells with important differentiation capacities are co-infused with the bone marrow grafts \(^7\)\(^8\).

Molecular studies of chimerism after BMT allowed the detection of rare, but authentic, leukemia of donor origin. Since the original description in 1971, more than 50 donor cell leukemia have been reported and considered as the result of oncogenic transformation of apparently normal donor hematopoietic cells in the transplant recipient \(^9\). Using fluorescent in situ hybridization (FISH), the contribution of donor human bone marrow cells to solid organ cancers after BMT has also been recently shown \(^10\)\(^11\). A recent murine study suggests that bone marrow-derived cells (BMDCs) contribute to cancer arising from the stomach lining \(^12\). Transplantation experiments performed in mice with chronic gastritis due to *Helicobacter* infection showed that resultant gastric carcinomas contained marrow-derived dysplastic and neoplastic glands. This study primarily emphasizes the importance of chronic inflammation in recruiting BMDCs.

Here we addressed the question of the donor or recipient origin of oral squamous cell carcinomas developed after allogeneic BMT. These rare human
tumors, without corresponding experimental model to date, have peculiar characteristics, with an aggressive behavior and poor prognosis, and a strong association with prior chronic lichenoid lesions of the oral mucosa \(^{13}\). In the context of BMT, recognizing the donor or recipient origin of oral SCC could lead to a better characterization of marrow stem cell transdifferentiation in humans, and possibly have implications for therapeutic management of engrafted patients.

**Patients and Methods**

**Patients**

From June 1976 to December 2006, 26 patients with allogeneic BMT were diagnosed with SCC. Eight of them had available frozen surgical samples. Five patients were transplanted in a sex-mismatched situation, three in a sex-matched situation. All were full donor hematopoietic chimera, without relapse, at the time of biopsy. Controls for FISH analyses were 6 cases of SCC in non-transplanted patients and 6 cases of SCC after sex-matched allogeneic BMT. Tissue samples were formalin-fixed surgical pieces with cryopreserved parts. Histological diagnosis had been established according to standard criteria and p53 staining \(^{14}\). The study has been approved by the institutional review board of the Hospital Saint Louis (Paris, France) and conducted with informed consent according to the Declaration of Helsinki.

**Combined FISH and immunostainings**

Combined FISH and immunostainings were performed on the same 5-\(\mu m\) thick sections (as described in \(^{15,16}\)). Briefly, anti-human CD45 (clone 2B11+PD7/26, Dako) or p53 (clone DO7, Dako) mouse antibody were used as primary antibodies before proteinase K digestion. FISH was performed using CEP X/Y DNA probes (Vysis), and followed by staining with anti-
human cytokeratin (clone AE1/AE3, Boehringer-Mannheim) or CD31 (clone JC70A, Dako) mouse antibody, and AMCA-conjugated anti-mouse IgG horse secondary antibody (Vector).

Tissue sections were analyzed by two different pathologists (AJ, HM) on a motorized Z-axis Olympus BX 61 microscope, alternatively using bright and epi-fluorescent light. Microscopic pictures obtained through a UPlan FI 100x/1.3NA objective were captured with a digital camera ColorView III using Olympus-SIS Cell F software.

For chromosomal analysis, inflammatory cells were characterized as CD45+, CD31- in the lamina propria, and CD45+, keratin- in the epithelium; endothelial cells as CD31+, CD45-; tumor cells as keratin+, p53+. X and Y signals were counted in a minimum of 200 cells for tumor cells, inflammatory infiltrate and non-tumoral epithelial or conjunctive cells, respectively. A correction factor was calculated by analyzing XY positive cells on male control tissues.

**Laser microdissection and short term repeated sequences (STR) PCR**

A minimum of 1000 cells of three types were successively and separately laser-microdissected (PALM, Bernried) on serial 7 μm-thick sections: tumor cells, normal epidermal cells and inflammatory cells. STR-PCR was performed after overnight proteinase K incubation at 56°C, without DNA extraction. 17 highly polymorphic STR sequences were amplified D1S225, D1S2892, D2S138, D3S1573, D6S264, D7S490, D8S261, D8S1820, D9S162, D11S860, D11S1356, D13S171, D16S496, D17S855, D17S1879, D18S61, and P53CA.
Results

From June 1976 to December 2006, 26 patients were diagnosed at Saint-Louis Hospital with oral SCC after allogeneic BMT. Tumors were identified by both microscopic morphological examination and immunostaining for p53, which we have previously shown to be stabilized in the vast majority of this type of tumors \(^{14}\). Five patients who had been transplanted in a sex-mismatched situation (donor and recipient from opposite sex), and three patients with a donor of the same sex (sex-matched) had available frozen surgical specimens. All these patients had received non-manipulated, non-T-cell depleted, bone marrow grafts.

In the sex-mismatched situation, combined FISH XY and immunohistochemical staining on the same tissue section of SCC samples showed that tumor cells of 2 out of the 5 sex-mismatched patients had a sexual genotype consistent with the donor (Table 1). One patient was a male with tumor cells of female genotype. The other patient was a female with tumor cells of male genotype. A thorough enquiry showed that she had never been pregnant, thus ruling out the possibility of chimeric male cells seeded during a previous male pregnancy (Table 2). We combined immuno-histochemical stainings with FISH XY to perform our genotype analysis on well-characterized cell populations. Reliable distinction, on tumor microscopic sections, of epithelial cells from endothelial and inflammatory cells, was of major importance since it has been reported that some endothelial cells of the tumor vasculature can, as inflammatory cells, differentiate from the donor hematopoietic stem cells \(^{17}\). Altogether, for the first case, a male recipient transplanted with female bone marrow, the tumor cells were of female genotype, as were inflammatory cells, whereas the normal epidermis, as capillary cells, were of male genotype (Fig. 1). In the second case, a female recipient transplanted with male bone marrow, the tumor cells and
inflammatory cells were of male genotype, whereas the endothelial cells and normal epidermal cells were of female genotype (Fig. 2).

To control these FISH studies by a completely different method, which also associated molecular markers and morphological selection of cell populations, we performed a microsatellite analysis of laser-microdissected tumor cells from cryocut sections of surgical pieces. We compared the profiles with those from laser-microdissected normal epidermis (from the recipient) and laser-microdissected inflammatory cells (from the donor) from other blocks of the same surgical pieces. We had to choose highly polymorphic short tandem repeat (STR) sequences for this STR-PCR analysis since all patients had received allogeneic BMT from their siblings. In the two patients with sex-mismatched BMT and donor-derived tumors, the laser-microdissected tumor cells were again established to be of donor genotype on three and two different alleles respectively (Fig. 1 and Fig. 2).

Three other patients who underwent BMT from a donor of the same gender were also studied by STR-PCR. In two of the three patients studied, respectively three and five STR-PCR profiles from laser-microdissected cells were identical for the tumor and the donor, but distinct from the recipient (Fig. 3), demonstrating the donor-derived origin of the epithelial cancer. Altogether, we provide conclusive evidence of epithelial tumor of donor cell origin in four patients with bone marrow transplantation.

We could perform this study on an exceptional set of patients, as SCC after BMT are rare, occurring in 1/500 long-term survivors. They develop on oral mucosa, with a highly aggressive behavior leading to death within few months despite early and large surgical removal. This is the case for the four patients we studied who developed SCC 5 to 22 years after BMT and died 6 to 12 months after oral SCC was diagnosed (Table 2). None had smoking or alcohol intoxication, in contrast to common oral SCC in non-grafted patients. But they all had a previous history of extensive chronic graft-versus-host
disease (GVHD) with oral mucosa involvement and they had needed a prolonged immunosuppressive therapy (18-42 months, mean 36 months).

Finally, we wondered if donor cell-derived cancer could occur in another solid tumor type (i.e. breast cancer). Among 6 such cases diagnosed in our institution, pathological material was available for only one case whose STR-PCR demonstrated a recipient origin (supplemental figure).

Discussion

Lichenoid lesions of oral mucosa are a characteristic feature of chronic GVHD after BMT 18, 19. At the tissular level, apoptosis of basal keratinocytes, the target cells of the alloimmune reaction, is associated with large, actively synthesizing keratinocytes at the upper levels of the epithelium 20. Such an association of cell damage and tissue repair features within the epithelium is characteristic of a lichenoid reaction 21. Kinetic studies using cell BrdU labeling have suggested that lichenoid reactions could be a form of squamous epithelial reaction to a chronic basal damage, whether immune-mediated, drug-induced or idiopathic 22. Moreover, the ulcerated form of idiopathic oral lichen planus is associated with a high risk of malignant transformation. In the context of chronic GVHD, the lichenoid lesion of the oral mucosa could favor malignant transformation. One of the four patients with donor-derived SCC also had Fanconi anemia, a disease characterized an increased risk of GVHD 23 and SCC 24. Of interest, microsatellite instability (MSI) at tetranucleotide repeats was detected in laser-microdissected colonic crypts and in buccal smears of 75% and 42%, respectively, of patients who received an allograft 25. MSI in clinically intact oral mucosa was more frequently found at later time points after HCT. MSI was also found in 3 post-transplant squamous cell cancers 25.

The occurrence of oral SCC, an epithelial tumor, of donor origin after BMT implies a supplementary step of transdifferentiation of marrow stem
cells in normal epidermal cells $^{3,16}$. The homing of these stem cells in the oral lesion of chronic GVHD could reflect their attraction to a zone of chronic inflammation and tissue repair $^{26,27}$. Moreover, the epithelial stem/progenitor cells might become exhausted by severe or chronic injury, and be replaced by circulating bone marrow-derived ones $^{16,28,29}$.

Interestingly, the skin is also the main site of development of cancers in patients after solid organ transplantation $^{30}$. As in patients after BMT, these cancers are very aggressive and always of SCC type $^{31}$. A single SCC of donor origin after kidney transplantation was reported $^{32}$. If the local environmental factors favor homing and subsequent transformation of marrow stem cell in the oral mucosa, a central immune dysfunction could also favor the development of SCC after BMT. Chronic GVHD is a syndrome characterized by alloreactivity and immunodeficiency, conditions that clearly favor tumor development. Immune deficiency linked to chronic GVHD is further enhanced by the treatment of chronic GVHD $^{1}$ and risk of tumor is higher with prolonged immunosuppression $^{33}$. GVHD-associated immunosuppression $^{34}$ also increases the susceptibility to viral pathogens. We previously reported that SCC in this setting could not reliably be linked to viruses either to Herpes viruses or Papilloma viruses $^{14}$. This is in contrast to Epstein-Barr virus-associated post transplant lymphoproliferative disorders (PTLD) $^{35}$ (reviewed in reference $^{9}$). Although we have characterized donor-derived endothelial cells in the context of acute GVHD $^{16}$ and others have reported donor-derived endothelial cells in other solid tumor type $^{17}$, we failed to detect donor-derived endothelial cells in the 8 SCC cases we studied.

Relevant to our clinical observations is the experimental model of epithelial gastric cancer originating from bone marrow-derived cells in the context of chronic infection with Helicobacter pylori. In this model BMDCs repopulate the gastric epithelium chronically infected by Helicobacter pylori progress through metaplasia to intraepithelial cancer $^{12}$. It has also been
shown that bone marrow cells contribute to epithelial neoplasias of the small bowel, colon, and lung, but not the skin. To further assess bone marrow cells contribution to epithelial cancer, these authors used mouse models of intestinal and lung neoplasias, which demonstrated that the hematopoietic stem cell and its progeny incorporate within cancer. In this study 3 patients had SCC (1 lung, 2 skin), and all 3 had history of GvHD. The relative contribution of donor cells to SCC varied from 0% (skin cancers) to 20% (lung cancer). The discrepancy with our results could be attributed to different locations (oral mucosa versus skin and lung), and different degrees of associated chronic inflammation. Arai et al. also reported a case of donor-derived SCC of the oral cavity after peripheral stem cell transplantation and chronic GvHD (assessed by FISH). In these two latter reports it should be noted that FISH only was used to assess the donor versus recipient origin of the cancer cells. In this study, we controlled the FISH results by a completely different method, which also associated molecular markers and morphological selection of cell populations, and performed a microsatellite analysis of laser-microdissected tumor cells.

However, the caveat of this study is that, as expected from human materials, we cannot demonstrate which bone marrow cell type gave rise to these cancers. One interpretation of our data could be the fusion of marrow stem cells to epithelial cells. The possible fusion of marrow stem cells to SCC cancer stem cells, or alternatively epithelial stem cells, could be followed by "reduction division", leading to cells that are less than tetraploid (though perhaps not purely diploid) and contain a mosaic of genetic elements of both donor and recipient. However, in our patients the issue on reduction division is unlikely because we did not found a mosaic of genetic elements (mixed origin). PCR of short tandem repeats (STRs), which are highly polymorphic markers, allowed a clear discrimination of the patient and of his/her sibling donors. Furthermore, in the four tumors, more than one (2, 3, 3 and 5) STR was found to be of donor origin, and we never observed any STR of recipient origin. Using the same STR analyses, substantial amounts (9%-72%) of donor
DNA were found in fingernail clippings from 9 of 21 recipients 2 years and more after transplantation 38. Through microdissection and PCR of STRs Flemming and coworkers also proved the donor origin of a de novo hepatocellular carcinoma in 2 patients after liver transplantation 39. Finally, another possibility is that these tumors might stem from mesenchymal stem cells that are co-infused with hematopoietic stem cells within the marrow graft. We cannot however test this hypothesis in human beings. Finally, since we recently described that breast cancers after transplantation and are not associated with chronic GvHD40, we studied with the same methods the only case with available archived tissues and proved the recipient origin of this breast cancer. However, it must be emphasized that a single case does not allow any general conclusion (i.e. development of cancer in donor cells only in the setting of chronic GvHD and of SCC type).

The characterization of these donor-derived oral epithelial tumors in patients with chronic GVHD has theoretical implications for model of cancer progression and clinical implications in the context of widening BMT indications, prolonged immunosuppression, and longer survival of the patients.

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Authors contribution: GS and AJ designed the study and wrote the manuscript; AJ, HM and CL analyzed the morphological data; HM, CL, JMC, LL, AD, MV, PR performed the experimental studies; EG provided clinical data; HdT, PB and JS provided essential support for study design and manuscript writing. The authors declare no conflicts of interest.
References

Table legend

**Table 1**
Combined FISH and immunostainings in patients with SCC after sex-mismatched, sex-matched allogeneic BMT, and in non-transplanted patients

**Table 2**
Patient and transplant characteristics of the 4 patients with donor-derived cancer

**Legends for figures**

**Figure 1:**

*Donor cell origin of an oral squamous cell carcinoma occurring after allogeneic bone marrow transplantation*

*Tumor of XX genotype occurring in a male patient having received BMT from a female donor:*

**A:** Hematoxylin and eosin staining. Epithelial tumor cells invading the lamina propria of the oral mucosa

**B:** Immunostaining with an antibody directed against P53. Nuclei of the basal layers of the squamous cell carcinoma are strongly positive (**C:** higher magnification of the delimited area on B).

**D-G:** Combined immunostainings with FISH methods for X chromosome (green signal) and Y chromosome (red signal).

- Tumor cells have a XX genotype on overlay D, as shown at higher magnification on G, and they are not stained with the Y-chromosome specific probe.
- Capillary cells (Cap, arrowheads on D and E) have a XY genotype on overlay D.
- Mononuclear CD-45 positive cells on E, have a XX genotype on overlay D, as shown by green arrows.

**H:** High magnification of P53-positive tumor cells (arrowheads) before (upper picture) and after laser-microdissection (lower picture).

**I:** Comparison of the profiles of laser-microdissected tumor cells, inflammatory cells (from the donor), and epidermal cells (from the recipient) from blocks of the same surgical piece. Microsatellite analysis at the D2S138 locus shows that the tumor microdissected cells, as the microdissected inflammatory cells of the donor are heterozygous at this locus (106 and 111 base peaks), whereas the microdissected normal epidermal cells of the recipient is homozygous (106 base peak). Microsatellite analysis of this locus,
and another one (D17S1879, not shown), demonstrate the donor origin of the tumor.

**Figure 2:**

**Donor cell origin of an oral squamous cell carcinoma occurring after bone marrow transplantation**

**Tumor of XY genotype occurring in a female patient having received BMT from a male donor (No previous male pregnancy)**

**A:** Combined FISH XY and immunostainings on the same tissue section with antibodies directed against P53 (brown) and cytokeratin (AE1/AE3 (blue), showing strong stainings of the tumor cells. Tumor: tumor area, delimited through a large broken line; Cap: capillary lumen in the dermis; inflammatory cells: surrounded by short broken lines, in the dermis. The P53/cytokeratin-positive tumor cells are of XY genotype, as shown with green and red arrows on the enlarged overlaid area.

**B:** High magnification of P53-positive tumor cells (arrowheads), surrounded by a yellow line before microdissection in the upper picture. The holes left after single cell laser microdissection of the same tumor cells are surrounded by the same yellow line and showed by arrow heads in the lower picture.

**C, D:** Comparison of the profiles of laser-microdissected tumor cells, inflammatory cells (from the donor), and normal epidermal cells (from the recipient) from blocks of the same surgical pieces shows profile of tumor cells of donor origin using D17S1879 (**C**) and D1S2892 (**D**) STR sequences. For the D17S1879 locus (**C**), the microdissected tumor cells are homozygous, as the inflammatory cells of donor origin (158 base peak), whereas the microdissected epidermal cells of recipient origin are heterozygous (154 and 158 base peaks). For the D1S2892 locus (**D**), the microdissected tumor cells and inflammatory cells of donor origin are similarly heterozygous (102 and 117 base peaks), whereas microdissected normal epidermal cells of recipient origin are differently heterozygous (102 and 125 base peaks).

**Figure 3:**

**Donor cell origin of an oral squamous cell carcinoma occurring after bone marrow transplantation demonstrated by STR-PCR of laser microdissected cells in 2 sex-matched transplant recipients**

**A:** Case III: First line: microscopic pictures of sequential cell by cell laser-microdissection of P53-positive tumor cells (arrows) first picture: P53 positive tumor cells are surrounded by a yellow line before laser microdissection; second picture: laser microdissection has been performed for the two upper tumor cells; third picture: laser microdissection has been performed for all surrounded P53 positive tumor cells. Following lines: microsatellite analyses using D8S261, D8S1820, and P53CA STR sequences. For the locus D8S261, the microdissected tumor cells and inflammatory cells of donor origin were...
similarly heterozygous (134 and 136 base peaks), whereas microdissected epidermal cells of recipient origin were differently heterozygous (128 and 140 base peaks). For the locus D8S1820, the microdissected tumor cells and inflammatory cells of donor origin were similarly heterozygous (104 and 106 base peaks), whereas microdissected epidermal cells of recipient origin were differently heterozygous (106 and 113 base peaks). For the locus P53CA, the microdissected tumor cells and inflammatory cells of donor origin were similarly heterozygous (122 and 124 base peaks), whereas microdissected epidermal cells of recipient origin were differently heterozygous (103 and 118 base peaks).

B: Case IV. First line: microscopic pictures of P53-positive tumor sheets invading the lamina propria (left picture), and at high magnification with successive steps of laser-microdissection (middle and right pictures). Following lines: microsatellite analyses using D7S490, D17S855 and D9S162 STR sequences. For the locus D7S490, the microdissected tumor cells and inflammatory cells of donor origin were similarly heterozygous (93 and 103 base peaks), whereas microdissected epidermal cells of recipient origin were differently heterozygous (106 and 117 base peaks). For the locus D17S855, the microdissected tumor cells and inflammatory cells of donor origin were similarly heterozygous (154 and 156 base peaks), whereas microdissected epidermal cells of recipient origin were differently heterozygous (145 and 154 base peaks). For the locus D9S162, the microdissected tumor cells and inflammatory cells of donor origin were similarly homozygous (181 base peak), whereas microdissected epidermal cells of recipient origin were heterozygous (181 and 191 base peaks).

Microsatellite analyses using D8S261, D13S171 STR sequences. For the locus D8S261, the microdissected tumor cells and the microdissected epidermal cells of recipient origin were similarly heterozygous (131 and 139 base peaks), whereas the microdissected inflammatory cells of donor origin were differently heterozygous (131 and 137 base peaks). For the locus D13S171, the microdissected tumor cells and the microdissected epidermal cells of recipient origin were similarly heterozygous (233 and 248 base peaks), whereas the microdissected inflammatory cells of donor origin were homozygous (238 base peak).
### Table 1. Combined FISH and immunostainings in patients with SCC after sex-mismatched, sex-matched allogeneic BMT, and in non-transplanted patients

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<td>% of positive cells</td>
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<sup>a</sup> correction factor of 1.34  
<sup>b</sup> correction factor of 1.47  
<sup>c</sup> correction factor of 1.41  
Correction factor is calculated on normal epithelium.

**Oral squamous cell carcinomas after sex-matched allogeneic BMT (Control I)**

<table>
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<th>Sex</th>
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<th>Inflammatory cells</th>
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**Oral squamous cell carcinomas without transplantation (Control II)**

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**Abbreviations:** BMT, bone marrow transplantation
### Table 2. Patient and transplant characteristics of the 4 patients with donor-derived cancer

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<th>Patient</th>
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<th>Age at diagnosis (years)</th>
<th>Treatment before transplant</th>
<th>Conditioning regimen</th>
<th>GVHD prophylaxis</th>
<th>Recipient Sex</th>
<th>Donor sex/ Relationship</th>
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<tr>
<td>III</td>
<td>Fanconi</td>
<td>4</td>
<td>Steroids, Androgens</td>
<td>Cy</td>
<td>MTX</td>
<td>F 0</td>
<td>F / Sibling</td>
<td>II</td>
<td>Ext</td>
<td>CsA, steroids</td>
<td>Oral</td>
<td>Died, cancer</td>
<td>12M</td>
</tr>
<tr>
<td>IV</td>
<td>ALL</td>
<td>43</td>
<td>Chemotherapy</td>
<td>Cy, VP16, TBI</td>
<td>MTX, CsA</td>
<td>M -</td>
<td>M / Sibling</td>
<td>II</td>
<td>Ext</td>
<td>CsA, steroids</td>
<td>Oral</td>
<td>Died, cancer</td>
<td>7M</td>
</tr>
</tbody>
</table>

**Abbreviations:** SAA, severe aplastic anemia; CML, chronic myelogenous leukemia; ALL, acute lymphoblastic leukemia; Cy, cyclophosphamide; TBI, total body irradiation; VP16, vepeside; MTX, methotrexate; TCD, T-cell depletion; CsA, cyclosporine; Ext, extensive, F, female; M, male; a Time interval: time interval between diagnosis and death
Case I. Male recipient / female donor
Tumor cells: XX; Inflammatory CD45+ cells: XX; Capillary cells: XY
Case II. Female recipient / male donor
Tumor cells: XY; Inflammatory CD45+ cells: XY; Capillary cells: XX
Figure 3

A

D8S261

D8S1820

P53CA

B

D7S490

D17S855

D9S162
Donor-derived oral squamous cell carcinoma after allogeneic bone marrow transplantation

Anne Janin, Hideyuki Murata, Christophe Leboeuf, Jean-Michel Cayuela, Eliane Gluckman, Luc Legres, Allison Desvreaux, Mariana Varna, Philippe Ratajczak, Jean Soulier, Hugues de The, Philippe Bertheau and Gerard Socie