Development of PCR Microchip for Early Cancer Risk Prediction

Sandeep Kumar Jha, Gi-Sung Joo, Gyu-Sik Ra, Hyun Ho Lee, and Yong-Sang Kim

***Abstract*—An integrated continuous-flow microfluidic chip was fabricated on glass substrate with polydimethylsiloxane (PDMS)-based microchannels, cell lysis and Polymerase chain reaction (PCR) modules on the same chip. While gold-microelectrode was used for electrochemical cell lysis, indium-tin-oxide (ITO) microheater was used for thermal cycling during PCR reaction. The fabricated device was used for PCR amplification of pancreatic cancer DNA marker (*SMAD4*) from non-tumorigenic MCF10a human cell lines. The PCR product (193 bp) was verified for MCF10a cells by agarose gel electrophoresis after 20 cycles of reaction on the microchip, whereas no product was detected in case of tumorigenic MCF7 cells. The total time required for the entire reaction was less than 45 min. Therefore, the proposed microchip can be helpful in predicting the risk of metastatic cancer by analysis of genetic tumor markers from human samples and can also be used for other genetic analysis involving PCR reaction.**

***Index Terms*—Electrochemical cell lysis, microfluidics, microheater, pancreatic cancer, polymerase chain reaction (PCR) microchip, polydimethylsiloxane (PDMS), SMAD4.**

I. Introduction

CANCER is amongst the largest cause of natural deaths worldwide. The genetic constitution of the human body plays a vital role in occurrence and progression of cancer. *SMAD-4* is amongst a few known genes to be determinant of causing high risk of cancer development. This gene is widely reported to be missing in up to 50% pancreatic cancer and 33% colorectal cancer tissues [1], [2]. Such deletion/mutation event takes place at the premalignant stage during progression of carcinoma into metastatic cancer [2]. The survivability of cancer patients increases drastically by early diagnosis of the disease [2] which is as elusive as a necessity. Such detection often involves tissue biopsy or expensive and unreliable tumor marker antigen study. In these conditions, analysis of genetic tumor markers by using Polymerase chain reaction (PCR) from tissue samples can be a more suitable approach. The PCR reaction, in general, is a widely used molecular biology technique for amplifying specific regions of DNA using DNA polymerase enzyme and is also applicable in cloning, genotyping, drugs discovery, forensic, environmental, and ever growing application areas.

The PCR analysis of template DNA is rather inexpensive; however, the instrumentation required for this purpose is quite costly. A typical PCR analysis requires a combination of reactions involving cell lysis, extraction of template DNA and PCR reaction, which is followed by analysis of PCR amplicon by gel electrophoresis. These steps are time consuming and labor extensive and require expensive chemicals. Therefore miniaturization of this technique as an inexpensive (after mass production) handheld-microchip is requisite for commercial as well as academic goals.

The Lysis of whole cells for extraction of DNA is a routine procedure in most of the biological laboratories. The known methods for this purpose are high voltage electroporation; proteinase-K, detergents and lysozyme treatment [3]; laser induced lysis [4]; bead milling and sonication [5], or freeze-thaw in liquid nitrogen [6]. Various attempts in the past were made towards the development of on-chip cell lysis device using different strategies. However, their methods lacked the aim of miniaturization. For example, a few groups have used extremely high voltage source (1–10 kV) [7], [8] or laser induced cell lysis [9] or methods needing sample pretreatment with additional reagents [10], [11]. On the contrary, our goal in the present study was to integrate a relatively inexpensive method for cell lysis that uses minimal reagents, power, and can be fabricated using common photolithographic techniques along with PCR module. The principle used for cell lysis was based on previous reports of applying a DC voltage to electrochemically generate hydroxide ion inside the device [12]. The electrochemically generated hydroxide ions permanently hydrolyze the cell membrane, thereby releasing intracellular genetic material [12], [13]. In continuation to this idea [13], the microchip was completely redesigned in the present study for reagent-less and power efficient complete lysis of cells. The device design was significantly different from previous reports where researchers carried on-chip cell lysis at the expense of costly cell lysis buffer [14] and had to use conventional thermal cycler for maintaining microchip temperature for PCR reaction [15].

Au-interdigitated electrodes were used for this purpose to input DC potential across the cells flowing through the microchannel and lysate was injected into the PCR module of the microchip [13]. The PCR module was fabricated on the

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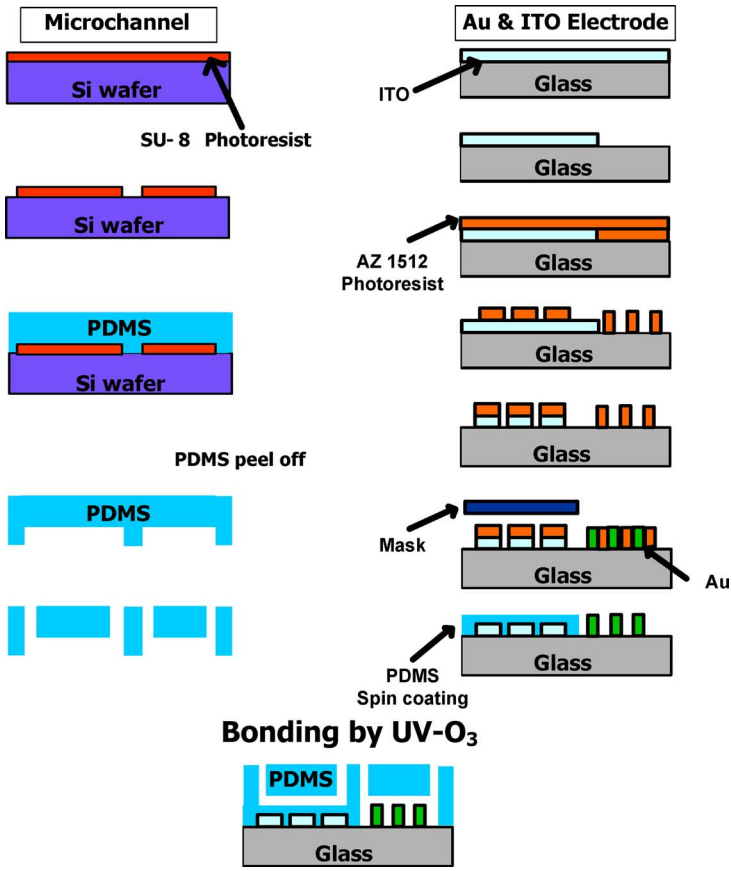


Fig. 1. Schematics for fabrication of cell lysis and PCR modules on glass substrate using the photolithographic technique.

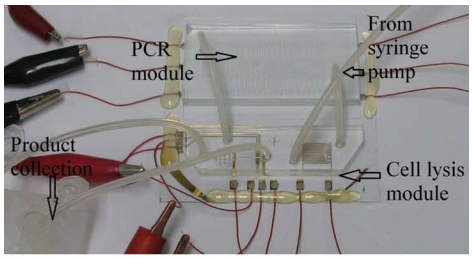
glass substrate using indium-tin-oxide (ITO) microheater and microchannels laid in the polydimethylsiloxane (PDMS) mold. The PDMS is widely used material for microfluidic devices because it can be easily and repeatedly fabricated by the negative molding method [16]; while the ITO heater electrodes were the choice for thermal cycling due to ease of its fabrication and linear and rapid variation of its temperature by application of DC power [16]. The cell lysis module was finally integrated with the micro-PCR device on the same glass substrate for on-chip PCR analysis of genomic DNA marker for pancreatic and colorectal cancer.

II. Methods

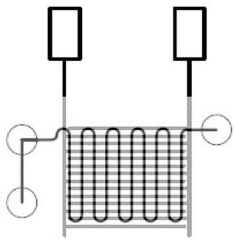
A. Device Fabrication

The entire microchip was developed on glass substrate. For this purpose, gold interdigitated microelectrodes for applying DC potential to the sample were fabricated over the glass by using photolithography and the evaporation method (Fig. 1). At first, photoresist AZ-1512 was spin-coated on glass and patterned using photolithography. After photolithography process, gold electrode was deposited using thermal evaporator. The electrode surface was cleaned with acetone and dried with N_2 gas. The microchannel was imprinted in the PDMS mold using the negative molding method (Fig. 1) [16]. For this purpose, 40 μm thick negative photoresist (SU-8 2075, Micro Chem.) was spin-coated and patterned on the silicon wafer. A degassed mixture of Sylgard 184 silicone elastomer along with curing agent (in 10:1 v/v ratio) was poured on the SU-8 patterned wafer and cured for 4 h at 72 °C. The PDMS mold formed was then peeled off manually and drilled to produce access holes of 3 mm diameter. The width and depth of the microchannel in the entire chip were 250 μm and 200 μm, respectively.

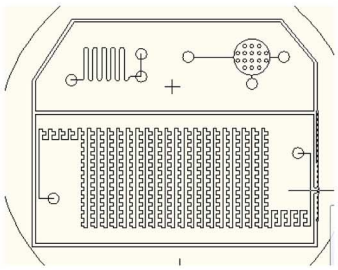
For fabrication of PCR module, the PDMS microchannel was fabricated once again by the negative molding method [16]. SU-8 was first spin-coated onto a bare silicon wafer and patterned to make microchannel using photolithography with mask aligner (MA-6, Karl-Suss) (Fig. 1). The degassed PDMS monomer mixture and curing agent (10:1 v/v) was poured on the SU-8 negative master pattern and cured for 4 h at 72 °C. The PDMS was then peeled off and manually drilled to produce access holes. The width and depth of the microchannel were once again 250 and 200 μm, respectively, and the total length of microchannel was 1550 mm including cell lysis module (114 mm) and for 20 PCR cycles (Fig. 2). The ratio of the channel lengths of the three different temperature zones for thermocycling, namely denaturation (92 °C), annealing (55 °C, and extension (73 °C was 2: 2: 3. It ensured a retention time of 30 s in denaturation and annealing zones and 45 s in the extension zone for PCR premix flowing in the microchannel at 5 μl/min rate. The PCR module was finally interconnected with the cell lysis module using silicone tubes inserted into drilled access holes.



(a)



(b)



(c)

Fig. 2. (a) The PCR microdevice: PDMS mold containing microchannels, electrical and inter-module microfluidic connections for cell lysis and PCR amplification; (b) schematics of cell lysis module: the interdigitated gold microelectrodes underlying the microchannel were used for electrochemical cell lysis; and (c) schematics of integrated PCR device showing microchannel arrangement in the modules.

The ITO heater electrode was the material of choice for thermal cycling due to its property showing linear variation of its temperature by application of DC power and was fabricated using conventional photolithography and wet etch process [17]. For this purpose, positive photoresist (AZ1512, Clariant) was spin-coated on glass with deposited ITO film (Samsung Corning) and then photoresist AZ1512 was patterned using photolithography to make ITO electrodes. The ITO film was then etched using $\mathrm{FeCl_3}$/HCl solution for 2 h and photoresist was removed [17]. For electrical isolation, a thin layer of PDMS was spin coated over microheater surface and baked at 95 °C for 30 min. ITO heaters were calibrated for liquid/air temperature control by inserting thermocouple into the microchannel during UV-ozone bonding. For finalizing the device fabrication steps, the PDMS mold and glass substrate containing ITO/Gold electrodes were bonded with each other by UV-ozone treatment for 40 min. Fig. 1 shows the schematics of fabrication process of continuous-flow PCR chip, while Fig. 2 illustrates the fabricated microchip.

B. Cultivation of Cells

The MCF10A cells were cultured in MEGM (Mammary Epithelial Growth Medium, Serum-free, Clonetics) supplemented with 100 ng/ml cholera toxin (Sigma) to 70% confluence as per method suggested by Caldas *et al.* [18]. The cells were harvested from culture plate by trypsinization and then centrifugation followed by washing with pH 7.4 phosphate buffer saline (PBS) twice and re-suspending (to 2×10^7 cells/ml concentration) in pH 7.4 PBS.

C. Cell Lysis

A suspension of 50 μl (10^6 cells/ml) cells from human cell line MCF10a/MCF7 in PBS was injected into the silicone tube carrying air in the microchannel using the precision syringe pump (KDS100, KD Scientific). The lysate was collected at the other end of the device (Fig. 2) and used in spectroscopic and agarose gel electrophoresis for confirmation of DNA release [13] or straightaway used in the PCR module. The cell lysate was analyzed for the presence of released genomic DNA using conventional 1% agarose gel electrophoresis. After electrophoretic separation, genomic DNA band was cut with a sterile knife and redissolved in Mega Spin™ gel elution kit (Intron Biotech., Korea) for spectroscopic analysis at 260 nm wavelength using an Eppendorf Biophotometer. For confirmation of PCR readiness of the extract, cell lysate was centrifuged to remove cell debris and thereafter, cell free extract was analyzed for presence of *SMAD4* gene using conventional PCR (Applied Biosystems Thermal cycler model 2720) technique using forward and reverse primers as GTCTATGGCACATCAAACTATGCACAATGC and GTCTAACAATTTTCCTTGCAACG respectively. After this verification regarding PCR-readiness of DNA template in the cell lysates, simultaneous on-chip electrochemical cell lysis and PCR reaction were performed.

D. On-Chip PCR Analysis

The fabricated devices were tested for on-chip simultaneous cell lysis and PCR reactions. At first, control experiment was performed to suggest success of the PCR module on the device by injecting a mixture of genomic DNA of λ-phage virus as template, PCR mix and the primers (forward: 5'-GCA-AGT-ATC-GTT-TCC-ACC-GT-3' and reverse: 5'-TTA-TAA-GTC-TAA-TGA-AGA-CAA-ATC-CC-3') in the microfluidic channel. A steady upstream thrust was maintained using airflow at a 5 μl/min rate and the PCR product was collected in a reservoir at the other end of the microchannel. The annealing temperature was kept at 55 °C in this case. The PCR product (100 bp) was collected at the other end of the microchannel in a reservoir and verified by 1% agarose gel electrophoresis.

The fabricated device was then used for lysis and PCR amplification of genomic DNA of nontumorigenic MCF10a and tumorigenic MCF7 human cell lines. For this purpose, approximately 10^6 cells of each cell lines were suspended in 50 μl PBS and 50 μl 2× PCR mix (Intron Biotechnology, Korea) containing Taq-DNA polymerase and 5 μl each of the primers (1 pmole/μl each) against *SMAD4* gene as described above were mixed with it. The mixture was injected into silicone tube carrying air to the microchannel with the help of the precision syringe pump. The PCR reaction was initiated with different temperature zones of 92 °C, 55 °C, and 68 °C for melting,

annealing, and extension, respectively, for 20 cycles. The PCR product (193 bp) was verified by 1% agarose gel electrophoresis with ethidium bromide as well as spectroscopic method.

A second control experiment was performed to suggest the usefulness of cell lysis module on the device by injecting PCR mix with MCF10a whole cells (in same proportions) directly into the PCR module rather than passing the mixture through cell lysis module.

III. Results and Discussion

In the present study, a low-cost cell lysis cum PCR device was fabricated using conventional photolithographic technique. The glass substrate was used to make transparent devices and for its suitability in bonding with PDMS by UV-ozone method [16]. The electrochemical lysis of cells from human cell line could be achieved between 2 and 5 V of DC input with optimum release of genomic DNA at 5 V for 5 min at a flow rate of 5 μl/min [13]. The alternate +5 and 0 V DC across 200 μm gap between the Au interdigitated electrode configuration helped in efficient cell lysis without the use of additional reagents. Observation of cell lysate on a haemocytometer with an optical microscope revealed complete lysis of cells under this condition. The process generated hydroxyl ions desired for lysis and at the same time, electrode impedance was low enough to avoid generation of Joule heat [19] inside the microchannel. Therefore, this method was supposed to yield cellular components in their native state. It also reduced dependence on microchannel preconditioning as used by various other groups [20], [21] and the hydrophobic PDMS wall also helped minimize the adherence of template DNA as well as PCR amplicon to the side walls of the microchannel. Since PBS buffer was used as carrier solvent, inhibitory components for PCR reaction such as SDS or triton-X100 as used inadvertently by various groups during cell lysis steps [20], could be eliminated.

Subsequently, the cell lysate from this module was verified for PCR level purity. For this, genomic DNA from MCF10a cell line was first extracted by on-chip lysis and then collected for conventional (off-chip) PCR amplification (30 cycles) using primer set against *SMAD4* gene [Fig. 3(a)]. A successful conventional PCR reaction with the cell lysates suggested the PCR readiness of template DNA in the mixture. Next, the device was tested for on-chip PCR amplification involving a control sample consisting of λ-phage genomic DNA. The commercially available λ-phage DNA in-fact did not require cell lysis. Yet, the PCR mixture was passed through the cell lysis module to verify any adverse effect of electrochemical cell lysis on PCR reaction (involving Taq DNA polymerase enzyme). The on-chip PCR amplification of this sample for a 20-cycles reaction successfully yielded the requisite 100 bp amplicon band in the agarose gel electrophoresis [Fig. 3(b)]. This suggested that integration of electrochemical cell lysis on the same PCR microchip was permissible, without any adverse effect on PCR reaction. The usefulness of integrating cell lysis with PCR modules on a single chip was demonstrated again with another control experiment, in which PCR mixed with MCF10a whole cells were injected directly into the PCR module rather than passing the mixture through the cell lysis module. It was though expected that the melting temperature used in PCR reaction could lyse the cells to release template DNA. However, this procedure did not yield PCR amplicon, at least not in the detectable range, as confirmed through gel electrophoresis and spectrophotometric methods. Therefore, it was an added benefit to integrate cell lysis and PCR modules on a single microchip for continuous operation with possibility to maintain asceptic condition.

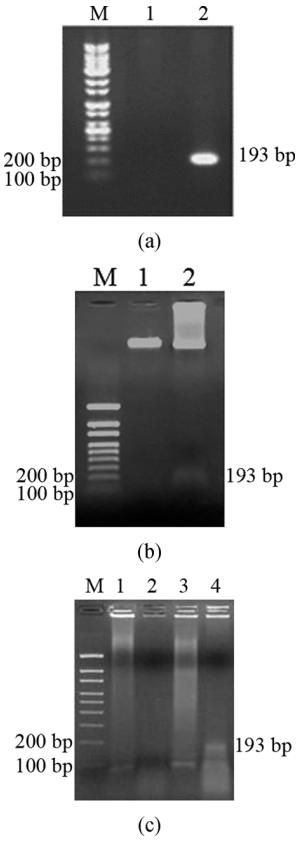


Fig. 3. (a) Gel-doc from analysis of *SMAD4* from MCF10a cells using 30 cycles of conventional PCR, lane M = 10 kb marker (Bionics, Korea), lane 1 = pre-PCR control, lane 2 = product from 30 cycles of conventional PCR reaction; (b) gel-doc of agarose gel electrophoresis of PCR products involving λ-phage DNA: flow rate 5 μl/min, lane M = 0.1 − 1.5 kb marker (Bionics, Korea), lane 1 = pre PCR mixture, lane 2 = PCR product; (c) gel-doc of agarose gel electrophoresis of PCR product involving *SMAD4* from MCF 7 and MCF 10a cells: flow rate 5 μl/min, lane M = 0.1 − 1.5 kb marker (Bionics, Korea), lane 1 = Pre PCR lysate for MCF7, lane 2 = PCR of MCF7, lane 3 = Pre PCR lysate for MCF10a, lane 4 = PCR of MCF10a.

The fabricated device was finally used for on-chip PCR amplification of genomic DNA from non tumorigenic MCF10a and tumorigenic MCF7 human cell lines by using the collected lysate from the cell lysis module and adding PCR mixture containing primers for tumor suppressor gene *SMAD4* [22] and Taq-DNA polymerase. The different temperature zones used for thermal cycling were 92 °C, 55 °C, and 68 °C for melting, annealing, and extension, respectively, for 20 cycles each. The liquid flowing through the microchannel thus had a retention time of 30 s in each zone at a flow rate of 5 μl/min. The total time required between addition of cell and PCR mix on the microchip and collection of PCR amplicon from the other end of device was less than 45 min. The benefit of having a flow-through microfluidic chip for PCR amplification as compared

to single drop static amplification models proposed by other groups [20], [21] was in efficient control of the temperature for PCR reactions. Also, it was easier to fabricate microchannels in a PDMS mold than conventional fluoride-etched all-glass microchip [23]. The PCR reaction as carried out by this process yielded desired 193 base pair product in case of MCF10a cells with a yield of approximately 250 ng DNA/10^6 MCF10a cells ($\mathrm{SD} = 25$ ng DNA, $\mathrm{n} = 3$) as also verified by agarose gel electrophoresis [Fig. 3(c)]; whereas, no product was detected in case of MCF7 cells. This demonstrated the successful application of the fabricated PCR microchip and suggested a possibility of early prediction of malignant pancreatic, colorectal, or similar cancers which progresses due to lack of the *SMAD4* gene in these particular tissues. As additional usage of the device, it can also be used in almost any other genetic analysis involving DNA extraction and PCR amplification in a rapid and cost-effective manner.

REFERENCES

[1] I. Schwarte-Waldhoff and W. Schmiegel, "*Smad4* transcriptional pathways and angiogenesis," *Int. J. Gastrointestinal Cancer*, vol. 31, pp. 47–59, 2002.

[2] M. W. Volmer, K. Stühler, M. Zapatka, A. Schöneck, S. Klein-Scory, W. Schmiegel, H. E. Meyer, and I. Schwarte-Waldhoff, "Differential proteome analysis of conditioned media to detect Smad4 regulated secreted biomarkers in colon cancer," *Proteomics*, vol. 5, pp. 2587–2601, 2005.

[3] Z. Lin and Z. Cai, "Cell lysis methods for high-throughput screening or miniaturized assays," *Biotechnol. J.*, vol. 4, pp. 210–215, 2009.

[4] R. B. Brown and J. Audet, "Current techniques for single-cell lysis," *J. R. Soc. Interface*, vol. 5, no. Suppl 2, pp. S131–138, 2008.

[5] E. Padilla, V. Gonzalez, J. M. Manterola, J. Lonca, A. Perez, L. Matas, M. D. Quesada, and V. Ausina, "Evaluation of two different cell lysis methods for releasing mycobacterial nucleic acids in the INNO-LiPA mycobacteria test," *Diagn. Microbio. Infect. Dis.*, vol. 46, pp. 19–23, 2003.

[6] S. A. Kim, J. A. Yoon, M. J. Kang, Y. M. Choi, S. J. Chae, and S. Y. Moon, "An efficient and reliable DNA extraction method for preimplantation genetic diagnosis: A comparison of allele drop out and amplification rates using different single cell lysis methods," *Fertil Steril.*, 2008.

[7] D. W. Lee and Y.-H. Cho, "A continuous electrical cell lysis device using a low dc voltage for a cell transport and rupture," *Sens. Actuators B Chem.*, vol. 124, pp. 84–89, 2007.

[8] J. Gao, X.-F. Yin, and Z.-L. Fang, "Integration of single cell injection, cell lysis, separation and detection of intracellular constituents on a microfluidic chip," *Lab Chip*, vol. 4, pp. 47–52, 2004.

[9] M. D. Dhawan, F. Wise, and A. J. Baeumner, "Development of a laser-induced cell lysis system," *Anal. Bioanal. Chem.*, vol. 374, pp. 421–426, 2002.

[10] C. Xing, C. Dafu, L. Changchun, and C. Haoyuan, "Microfluidic biochip for blood cell lysis," *Chin. J Anal. Chem.*, vol. 34, pp. 1656–1660, 2006.

[11] H. J. Lee, J.-H. Kim, H. K. Lim, E. C. Cho, N. Huh, C. Ko, J. C. Park, J.-W. Choi, and S. S. Lee, "Electrochemical cell lysis device for DNA extraction," *Lab Chip*, vol. 10, pp. 626–633, 2010.

[12] D. Di Carlo, C. Ionescu-Zanetti, Y. Zhang, P. Hung, and L. P. Lee, "On-chip cell lysis by local hydroxide generation," *Lab Chip*, vol. 5, pp. 171–178, 2005.

[13] S. K. Jha, G.-S. Ra, G.-S. Joo, and Y.-S. Kim, "Electrochemical cell lysis on a miniaturized flow-through device," *Current App. Phys.*, vol. 9, pp. e301–e303, 2009.

[14] C. Ke, A.-M. Kelleher, H. Berney, M. Sheehan, and A. Mathewson, "Single step cell lysis/PCR detection of Escherichia coli in an independently controllable silicon microreactor," *Sens. Actuators B*, vol. 120, pp. 538–544, 2007.

[15] L. C. Waters, S. C. Jacobson, N. Kroutchinina, J. Khandurina, R. S. Foote, and J. M. Ramsey, "Microchip device for cell lysis, multiplex PCR amplification, and electrophoretic sizing," *Anal. Chem.*, vol. 70, no. 1, pp. 158–162, 1998.

[16] J.-H. Kim, K.-H. Na, C. J. Kang, and Y.-S. Kim, "A disposable thermopneumatic-actuated micropump stacked with PDMS layers and ITO-coated glass," *Sens. Actuators A: Phys.*, vol. 120, pp. 365–369, 2005.

[17] S.-R. Joung, J.-H. Kim, I. J. Yi, C. J. Kang, and Y.-S. Kim, "Series DNA amplification using the continuous-flow polymerase chain reaction chip," *Jpn. J. Appl. Phys.*, vol. 47, pp. 1342–1345, 2008.

[18] H. Caldas, L. E. Honsey, and R. A. Altura, "Survivin 2α: A novel Survivin splice variant expressed in human malignancies," *Mol. Cancer*, vol. 4, p. 11, 2005.

[19] Y. Zhang, N. Bao, X.-D. Yu, J.-J. Xu, and H.-Y. Chen, "Improvement of heat dissipation for polydimethylsiloxane microchip electrophoresis," *J. Chromatography A*, vol. 1057, pp. 247–251, 2004.

[20] L. C. Waters, S. C. Jacobson, N. Kroutchinina, J. Khandurina, R. S. Foote, and J. M. Ramsey, "Microchip device for cell lysis, multiplex PCR amplification, and electrophoretic sizing," *Anal. Chem.*, vol. 70, pp. 158–162, 1998.

[21] J. W. Hong, T. Fujii, M. Seki, T. Yamamoto, and I. Endo, "Integration of gene amplification and capillary gel electrophoresis on a polydimethylsiloxane-glass hybrid microchip," *Electrophoresis*, vol. 22, pp. 328–333, 2001.

[22] S. Ali, C. Cohen, J. V. Little, J. H. Sequeira, M. B. Mosunjac, and M. T. Siddiqui, "The utility of *SMAD4* as a diagnostic immunohistochemical marker for pancreatic adenocarcinoma, and its expression in other solid tumors," *Diagn. Cytopathol.*, vol. 35, pp. 644–8, 2007.

[23] M. U. Kopp, A. J. de Mello, and A. Manz, "Chemical amplification: Continuous-flow PCR on a chip," *Science*, vol. 280, pp. 1046–1048, 1998.

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