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PROTOCOL

Cultures of biopsy-derived skin fibroblasts

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This paper is described in a single column, which is better to be read by researchers on lab benches, and is our note available only in our laboratory. The protocol has been approved by the ethical committee in the TMC.

ABSTRACT

Alzheimer′s disease (AD) is likely a systemic disorder. Molecules relevant to AD pathology, which we think are neuron-specific, are not just restricted to the brain. This suggests that biological, metabolic, biochemical, molecular, and pharmacological abnormalities of cells characteristic of AD may be observed in peripheral cells. Examples of such peripheral cells are skin fibroblasts. Skin fibroblasts have successfully been used to test hypotheses on the primary pathological mechanisms leading to AD and are therefore expected to provide useful biological markers and promising therapeutic strategies. Consistent protocols for culturing skin fibroblasts among laboratories would facilitate the comparison of data from fibroblasts worldwide and enable the use of fibroblasts as reliable and significant biological markers of AD. Tottori J. Clin. Res. 9(1), 56-76, 2017

Key words: Alzheimer′s disease, skin biopsy, skin fibroblasts, biological markers

INTRODUCTION

A growing body of evidence has revealed that the whole body, and not just the brain, is involved in AD pathology[1–3]. A number of abnormalities in metabolic and biochemical processes, including β-amyloid precursor protein (βAPP) processing, tau metabolic pathways, and intracellular signal transduction, which are relevant to brain dysfunction in AD patients, are found in skin fibroblasts[4], lymphocytes[5], platelets[6,7], endothelial cells[7], lenses[8], skeletal muscles[9], olfactory epithelial cells[10], and olfactory sensory neurons[11]. This suggests the possibility that AD constitutes a widespread, systemic disorder[12,13], although the clinical phenotypic expression of AD is mostly brain specific[14].

Good examples of the successful use of peripheral cells to examine biological, metabolic, biochemical, molecular, and pharmacological abnormalities in the cells of AD patients are studies on βAPP processing and signal transduction systems, mostly performed on fibroblasts[2–4,13–16]. Within this context, data obtained using fibroblasts help to identify and test primary pathological mechanisms leading to AD[17], thereby providing useful biological markers[2,3,14,18–20] and promising therapeutic strategies[21]. In addition, recent developments in induced pluripotent stem cells (iPSCs) and induced neurons from skin fibroblasts have allowed in vitro investigation of phenotypes of AD[22,23].

We described here a detailed protocol for culturing skin biopsy-derived fibroblasts[2,3,14,18–21] to identify biomarkers of AD and assess their suitability and accuracy as diagnostic markers of AD and disease progression[24].

MATERIALS

Reagents:

- 69% nitric acid (Wako, 143-01326)