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Supplementary Data

Spatiotemporal Complexity of Fibroblast Networks Screens for Alzheimer's Disease

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7	2	6
4	1	5
8	3	9

Supplementary Figure 1. Standard operation procedures for image acquisition per well.

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Supplementary Table 1
In-depth demographics, genetic/family history, and clinical history of the Banked patients*

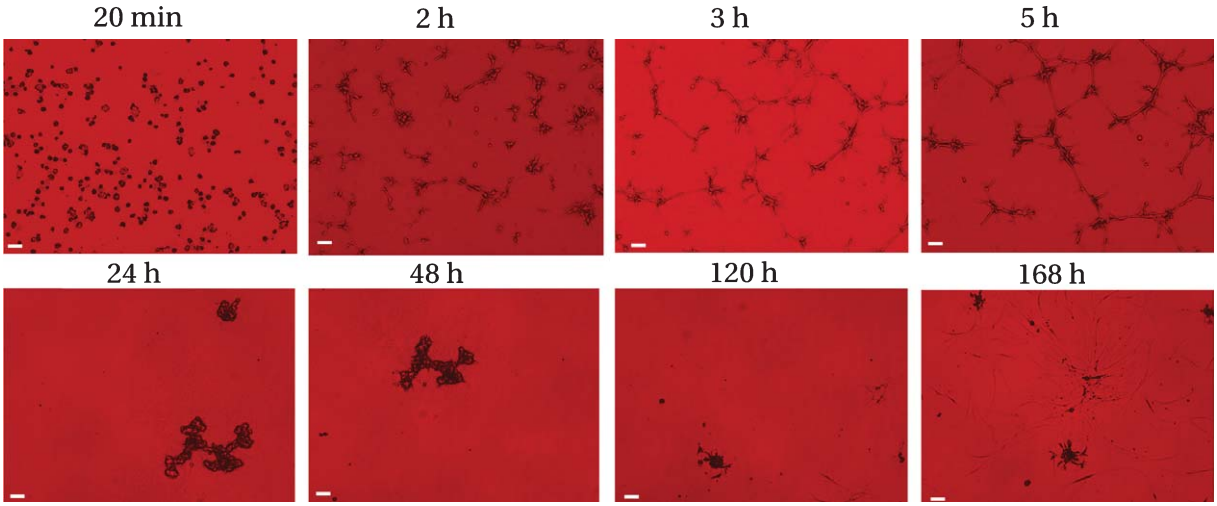
Cell ID	Demographic, age (y), gender (M/F), genetic/family history, clinical diagnosis, biopsy source
Aged-matched Control (AC) ($n = 11$)	
AG12438	Caucasian, 77, M, non-demented. The skin biopsy was taken antemortem
AG12927	Caucasian, 66, F, non-demented. The skin biopsy was taken antemortem
AG07714	Caucasian, 56, F, non-demented. The skin biopsy was taken antemortem
AG04146	Caucasian, 57, M, non-demented. The skin biopsy was taken antemortem
AG11734	Caucasian, 50, F, non-demented. The skin biopsy was taken antemortem
AG05840	Caucasian, 55, F, non-demented. The skin biopsy was taken antemortem
AG07123	Caucasian, 62, M, non-demented. The skin biopsy was taken antemortem
AG09977	Caucasian, 63, F, non-demented. The skin biopsy was taken antemortem
AG12998	Caucasian, 65, M, non-demented. The skin biopsy was taken antemortem
AG11358	Caucasian, 71, M, non-demented. The skin biopsy was taken antemortem
AG04461	Caucasian, 66, M, non-demented. The skin biopsy was taken antemortem
Alzheimer's Disease (AD) ($n = 13$)	
AG05770	Caucasian, 70, M, no family history of AD. 7.5 y of disease duration before the biopsy, autopsy confirmed AD. The skin biopsy was taken postmortem
AG08245	Caucasian, 75, M, no family history of AD. 7 y of disease duration before the biopsy, autopsy confirmed AD. The skin biopsy was taken postmortem
AG06263	Caucasian, 67, F, no family history of AD. This is a sporadic AD case by clinical diagnosis. 7 y of disease duration. The skin biopsy was taken antemortem
AG08170	Canadian Caucasian, 56, M, clinically confirmed familial AD. History of progressive memory loss beginning at age 55 y. The skin biopsy was taken antemortem
AG06840	Canadian Caucasian, 56, M, clinically confirmed familial AD with presenilin 1 gene. History of progressive memory loss of 1 y. The skin biopsy was taken antemortem
AG04159	Canadian Caucasian, 52, F, clinically confirmed familial AD. History of progressive memory loss. The skin biopsy was taken antemortem
AG06844	Canadian Caucasian, 59, M, autopsy confirmed familial AD. The skin biopsy was taken antemortem
AG06869	Caucasian, 60, F, no family history of AD, confirmed at autopsy. Disease duration of 1 y. The skin biopsy was taken antemortem
AG07374	Caucasian, 73, M, no family history of AD, clinically confirmed. The skin biopsy was taken antemortem
AG08527	German Caucasian, 61, M, autopsy confirmed AD. The skin biopsy was taken antemortem
AG10788	Caucasian, 87, gender was not reported. Autopsy confirmed AD with 17 y of disease duration. Family history of AD with ApoE4 gene. The biopsy was taken antemortem
AG11368	German Caucasian, 77, M, autopsy confirmed and family history of AD. Minced skin tissue was taken for establish fibroblasts culture
AG05810	Jewish Caucasian, 79, F, clinically confirmed late-onset AD with a profound familial aspect. Three sibs died with autopsy confirmed AD with ApoE gene. The biopsy was taken antemortem
Non-Alzheimer's Disease dementia (non-ADD) ($n = 9$)	
GM02173	Caucasian, 52, F, clinically confirmed and genetically validated Huntington's disease**
GM00305	Caucasian, 56, F, clinically confirmed Huntington's disease with unknown family history of nervous system disorder**
GM05030	Caucasian, 56, M, choreic movements with clinically confirmed and genetically validated Huntington's disease**
GM05031	Caucasian, 60, M, clinically confirmed and genetically validated Huntington's disease**
GM06274	Caucasian, 56, F, clinically confirmed and genetically validated Huntington's disease**
GM02165	Caucasian, 57, M, clinically confirmed and genetically validated Huntington's disease**
GM02167	Caucasian, 59, F, clinically confirmed and genetically validated Huntington's disease**
ND27760	Caucasian, 55, F, clinically affected familial Parkinson's disease with mutation in PARK1 gene**
AG08395	Caucasian, 85, F, autopsy confirmed Parkinson's disease. The skin biopsy was taken postmortem

*All information are obtained from the Coriell Cell Repository.
**The time of biopsy taken was not reported whether it was antemortem or postmortem.

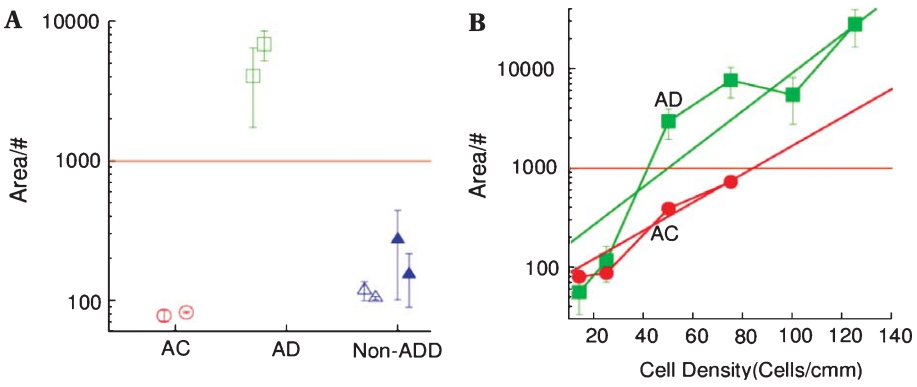
Supplementary Table 2
Performance parameters: accuracy, specificity, sensitivity, positive predictive value, and negative predictive value

Method	Accuracy (%)	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
Average area per number of aggregates	100	100	100	100	100
Fractal analysis	97	92*	100	100	95
Lacunarity analysis	95	100	100	90	100
Cell migration analysis	96	100	94**	90	100

*With 95% confidence interval 83% to 100%.
**With 95% confidence interval 86% to 100%.
The confidence intervals to the sensitivity and specificity were calculated step by step described by a well-known method (http://www.wikihow.com/Calculate-95%25-Confidence-Interval-for-a-Test%27s-Sensitivity).



Supplementary Figure 2. Alzheimer's disease (AD) fibroblast dynamics on a thick layer of 3-D matrix. Fast (top row) and slow (bottom row) dynamics are presented. Cellular aggregates are shown at 24 h and 48 h. Age-matched control (AC) cell lines exhibited a similar dynamics but qualitatively and quantitatively different. AC cell lines showed more cellular aggregates and of a smaller size at 24 and 48 h (Figs. 1D, 2B, and 3B). Scale bar is 10 μm.



Supplementary Figure 3. A) Test-to-test variation of the results for average area per number of aggregates: AC ($n = 1$), AD ($n = 1$), non-Alzheimer's disease dementia (non-ADD) ($n = 2$). Experiments were at least one month apart for the same cell lines. Initial number of cells was within 10%. B) Dependence of area per number of aggregates on initial cell density is exponential (solid lines), with a steeper rise for AD than for AC. Error-bars represent the standard deviation. Fit function is $f(x) = a * exp(x/b)$ where a = 112.8 and b = 22.8 for AD and a = 64.1 and b = 30.5 for AC. This representation suggests that for a cell density of 50 cells/mm^3 the separation is reasonably good for screening AD.