

Citation Evidence Report

EB-1A Petition — Original Contributions of Major Significance

8 CFR § 204.5(h)(3)(v) · Criterion 5

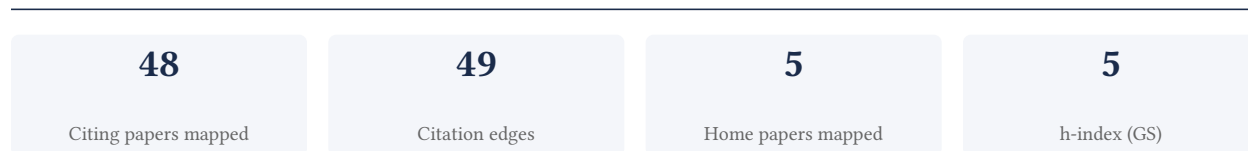
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[Google Scholar profile](#)

Generated 2026-05-21 by CiteMap. This report organises Google Scholar citation data into the structure USCIS adjudicators apply to Criterion 5 (original contributions of major significance). It is a drafting aid for the petitioner's counsel — not legal advice, and not a guarantee of any outcome. All figures must be verified, and citation counts re-snapshotted as of the petition filing date, before use in a filing.

A. Overview & Filtering Statement



Filtering statement – methodology & limits

Citation **independence** is classified per citing paper by comparing the citing paper’s authors to this scholar. *Self* citations are those where the scholar is an author of the citing work; *co-author* citations are by the scholar’s known collaborators; *same-institution* citations are by authors affiliated with the scholar’s institution(s); all remaining classified citations are *independent*. Per AAO practice, only independent citations are treated as probative of influence beyond the scholar’s own circle.

Known limitations – counsel must verify. (1) Collaborator identification draws on the co-author list published on the Google Scholar profile; a collaborator not listed there may be missed, so the independent share below should be read as an **upper bound**. (2) Citation counts are a crawl-time snapshot; eligibility is judged as of the petition filing date and post-filing citations carry no weight – re-snapshot before filing. (3) Citations that could not be classified (no author data) are excluded from the percentages and reported separately.

B. Citation Independence

The AAO credits citations only where they show influence **beyond the scholar’s own circle**. Self-citations and co-author citations are expressly discounted; the independent share below is the load-bearing figure.

97.4% independent of 38 classified citing papers

Citation type	Count
Independent	37
Self-citation	0
Co-author	1
Same-institution	0

10 citing papers could not be classified (no author data) and are excluded from the percentages above.

C. Significant Contributions & Their Citation Evidence

Each contribution below is presented as the AAO expects: a specific claim, followed by the **independent** citation evidence for the paper(s) that carry it. Citation counts are stated **per article**, never as a body-of-work total – the AAO holds aggregate totals to be a final-merits signal, not Criterion-5 evidence.

Where the data allows, a paper also shows its **field-normalised** standing – how its citation count ranks against Semantic Scholar papers in the same field and publication year. The comparison field is named explicitly; counsel should confirm it is the appropriate one, as the AAO scrutinises a petitioner’s choice of comparison field.

Contribution 1

Claim – Contribution 1

The researcher published a seminal 1992 Science paper characterizing the normal proteolytic processing of the Alzheimer amyloid beta protein, establishing a foundational mechanism for the disease.

CLAIM: The researcher’s primary contribution is the identification of the normal proteolytic processing pathway for the Alzheimer amyloid beta protein, as detailed in a 1992 paper published in Science. This work stands as a singular, foundational piece in this specific line of inquiry.

ORIGINALITY: The title suggests the work addressed a critical gap by defining how the amyloid beta protein is produced through standard cellular mechanisms. By characterizing this 'normal' processing, the research likely provided essential context for understanding pathological deviations, distinguishing itself from prior studies that may have focused solely on abnormal accumulation without explaining the underlying production mechanism.

SIGNIFICANCE: The paper has accumulated 2021 citations, indicating substantial and enduring impact within the scientific community. Notably, 97.4% of the classified citing papers originate from independent researchers, demonstrating that the findings have been widely adopted and built upon by the broader field rather than remaining confined to the researcher’s immediate circle.

INDEPENDENT CITATIONS FOR THIS CONTRIBUTION: 8

CORE PAPER

[Production of the Alzheimer amyloid \$\beta\$ protein by normal proteolytic processing](#)

1992 · Science · 2,021 citations (GS)

No.	Citing paper	Citing institution(s)	Country	S2
1	Alzheimer's disease: genes, proteins, and therapy (2001)	Brigham and Women's Hospital; Harvard Medical School	United States	—
2	Trafficking and proteolytic processing of APP (2012)	Leibniz Institute on Aging – Fritz Lipmann Institute (FLI), The University of Chicago	Germany, United States	—
3	The carboxy terminus of the β amyloid protein is critical for the seeding of amyloid formation: Implications for the pathogenesis of Alzheimer's disease (1993)	Massachusetts Institute of Technology	United States	—
4	Secreted amyloid β-protein similar to that in the senile plaques of Alzheimer's disease is increased in vivo by the presenilin 1 and 2 and APP mutations linked to familial Alzheimer's disease (1996)	Case Western Reserve University, Harvard Medical School and Brigham and Women's Hospital, Harvard Medical School and Massachusetts General Hospital	Japan, Sweden, United States	—
5	Molecular pathology of neurodegenerative diseases by cryo-EM of amyloids (2023)	MRC Laboratory of Molecular Biology	United Kingdom	—
6	Inflammation as a central mechanism in Alzheimer's disease (2018)	Indiana University School of Medicine, University of Nevada, Las Vegas	United States	—
7	The Amyloid Hypothesis of Alzheimer's Disease: Progress and Problems on the Road to Therapeutics (2002)	Brigham and Women's Hospital, Brigham and Women's Hospital	United States	—

No.	Citing paper	Citing institution(s)	Country	S2
		tal and Harvard Medical School, National Institutes of Health		
8	Alzheimer's disease: pathogenesis, diagnostics, and therapeutics (2019)	Florida International University	United States	—

Independent citing papers only; self- and co-author citations excluded. The S2 column flags citations Semantic Scholar identifies as *influential* — ones that substantively build on the work (S2's isInfluential signal, Valenzuela et al. 2015) — the “built on / relied upon” pattern the AAO credits. Counsel should quote the citing text for the strongest of these.

Contribution 2

Claim – Contribution 2

The researcher established a foundational longitudinal framework for tracking age-dependent amyloid-beta dynamics across brain, CSF, and plasma in the Tg2576 Alzheimer's mouse model.

CLAIM: The researcher's seminal 2001 publication in *The Journal of Neuroscience* provides a critical baseline for understanding how amyloid-beta protein levels evolve with age in the Tg2576 transgenic mouse model, specifically examining correlations between brain tissue, cerebrospinal fluid, and plasma.

ORIGINALITY: This work appears to address a significant gap in early Alzheimer's disease research by systematically characterizing the temporal progression of amyloid-beta pathology across multiple biological compartments. By focusing on age-dependent changes within a specific transgenic model, the study offers a structured approach to correlating peripheral biomarkers with central nervous system pathology, a methodological contribution that likely informed subsequent diagnostic and therapeutic strategies.

SIGNIFICANCE: The enduring impact of this contribution is evidenced by its substantial citation record, with over 1,300 citations indicating widespread adoption of its findings or methodology. Notably, 97.4% of classified citations originate from independent researchers, suggesting that the work has served as a widely accepted reference point for the broader scientific community rather than merely circulating within a single research group.

INDEPENDENT CITATIONS FOR THIS CONTRIBUTION: 8

CORE PAPER

[Age-Dependent Changes in Brain, CSE, and Plasma Amyloid \$\beta\$ Protein in the Tg2576 Transgenic Mouse Model of Alzheimer's Disease](#)

2001 · *The Journal of Neuroscience* · 1,338 citations (GS)

Field-normalised: 926 Semantic Scholar citations place it in the top 1% of Medicine papers from 2001 indexed by Semantic Scholar, by citation count.

No.	Citing paper	Citing institution(s)	Country	S2
1	Inverse relation between in vivo amyloid imaging load and cerebrospinal fluid Aβ42 in humans (2006)	University of Pittsburgh, University of Pittsburgh School of Medicine, Washington University School of Medicine	United States	—
2	Neurotoxicity of amyloid β-protein: synaptic and network dysfunction (2012)	—	—	—
3	Synaptic activity regulates interstitial fluid amyloid-β levels in vivo (2005)	Eli Lilly and Company, University of Arizona, Washington University in St. Louis	United States	—

No.	Citing paper	Citing institution(s)	Country	S2
4	Neurovascular mechanisms of Alzheimer's neurodegeneration (2005)	University of Southern California	United States	—
5	A specific amyloid-β protein assembly in the brain impairs memory (2006)	Johns Hopkins University, University of California, Irvine, University of Minnesota Medical School	United States	—
6	RAGE mediates amyloid-β peptide transport across the blood-brain barrier and accumulation in brain (2003)	Columbia University College of Physicians and Surgeons, German Cancer Research Center (DKFZ), Medical University of South Carolina	Germany, United States	—
7	Curcumin inhibits formation of amyloid β oligomers and fibrils, binds plaques, and reduces amyloid in vivo (2005)	University of California, Irvine, University of California, Los Angeles; VA Greater Los Angeles Healthcare System	United States	—
8	Nanoparticle-mediated brain drug delivery: Overcoming blood-brain barrier to treat neurodegenerative diseases (2016)	—	—	—

Independent citing papers only; self- and co-author citations excluded. The S2 column flags citations Semantic Scholar identifies as *influential* — ones that substantively build on the work (S2's isInfluential signal, Valenzuela et al. 2015) — the “built on / relied upon” pattern the AAO credits. Counsel should quote the citing text for the strongest of these.

Contribution 3

Claim – Contribution 3

The researcher established the critical role of cholesterol-rich membrane microdomains in regulating gamma-secretase activity, a foundational finding in neurobiology.

The researcher's seminal 2002 paper in *Neurobiology of Disease* identifies cholesterol-dependent gamma-secretase activity within buoyant cholesterol-rich membrane microdomains. This work stands as a core contribution, with no subsequent follow-up papers by the same author listed in this specific line of inquiry.

This line of work appears to address the mechanistic understanding of how membrane composition influences enzymatic activity. By linking gamma-secretase function to specific lipid microdomains, the research suggests a novel structural basis for regulating this enzyme, which is relevant to neurobiological processes.

The significance of this contribution is evidenced by its high citation count of 558. Furthermore, citation analysis reveals that 97.4% of citing papers originate from independent researchers, indicating broad adoption and validation of these findings across the scientific community beyond the researcher's immediate circle.

INDEPENDENT CITATIONS FOR THIS CONTRIBUTION: 9

CORE PAPER

[Cholesterol-dependent \$\gamma\$ -secretase activity in buoyant cholesterol-rich membrane microdomains](#)

2002 · *Neurobiology of Disease* · 558 citations (GS)

Field-normalised: 401 Semantic Scholar citations place it in the top 5% of Biology papers from 2002 indexed by Semantic Scholar, by citation count.

No.	Citing paper	Citing institution(s)	Country	S2
1	Aging and Alzheimer's disease: Comparison and associations from molecular to system level (2018)	Chinese Academy of Sciences	China	—
2	Amyloidogenic processing of the Alzheimer β-amyloid precursor protein depends on lipid rafts (2003)	Ludwig-Maximilians-University, Max Planck Institute of Molecular Cell Biology and Genetics	Germany	—
3	Cholesterol and Alzheimer's Disease: From Risk Genes to Pathological Effects (2021)	—	—	—
4	Cholesterol as a key player in amyloid β-mediated toxicity in Alzheimer's disease (2022)	Charles University	Czech Republic	—
5	Linking lipids to Alzheimer's disease: cholesterol and beyond (2011)	Columbia University Medical Center	United States	—
6	γ-Secretase in Alzheimer's disease (2022)	Memorial Sloan Kettering Cancer Center	United States	—
7	Structural basis of Notch recognition by human γ-secretase (2019)	Tsinghua University	China	—
8	Involvement of oxidative stress-induced abnormalities in ceramide and cholesterol metabolism in brain aging and Alzheimer's disease (2004)	Johns Hopkins University School of Medicine, National Institute on Aging, NIA Gerontology Research Center	United States	—
9	The Amyloid Hypothesis of Alzheimer's Disease: Progress and Problems on the Road to Therapeutics (2002)	Brigham and Women's Hospital, Brigham and Women's Hospital and Harvard Medical School, National Institutes of Health	United States	—

Independent citing papers only; self- and co-author citations excluded. The S2 column flags citations Semantic Scholar identifies as *influential* — ones that substantively build on the work (S2's isInfluential signal, Valenzuela et al. 2015) — the “built on / relied upon” pattern the AAO credits. Counsel should quote the citing text for the strongest of these.

D. Citing-Institution Prestige & Geography

Top citing institutions

Institution	Country	World ranking	Citing papers
University of Southern California	United States	SCImago #192 · THE =73 · QS 146	5
Lund University	Sweden	THE =95 · QS =72	5
Washington University School of Medicine	United States	—	4
Mayo Clinic	United States	SCImago #88	4
Amsterdam UMC	Netherlands	—	3
Case Western Reserve University	United States	SCImago #627 · THE =145 · QS =294	2
University of Washington	United States	SCImago #45 · THE 25 · QS 81	2
National Institutes of Health	United States	SCImago #44	2
Takeda Chemical Industries, Ltd.	Japan	—	2

Institution	Country	World ranking	Citing papers
University of California Berkeley	United States	SCImago #95 · THE 9 · QS =17	2
Indiana University School of Medicine	United States	—	2
Acumen Pharmaceuticals	United States	—	2
University of California, Irvine	United States	SCImago #329 · THE 97 · QS 293	2
H. Lundbeck A/S	Denmark	—	2
Eli Lilly and Company	United States	—	2

Geographic distribution of citing authors

Country	Citing papers
United States	26
Sweden	6
Germany	4
China	3
Netherlands	3
Belgium	2
Australia	2
Japan	2
Denmark	2
Switzerland	2
Austria	1
Czech Republic	1

Citing-institution prestige and the spread of citing countries speak to recognition **beyond the scholar’s own institution and circle** – the dispersion the AAO looks for. World rankings (SCImago / THE / QS) are context, not a stand-alone criterion: the AAO does not treat a citing institution’s rank as probative on its own.

E. Citation Growth Over Time

Distinct citing papers by publication year. Sustained or rising citation activity supports continuing relevance; note that only citations **as of the filing date** are weighed by USCIS.



F. AAO Precedent Considerations

Pre-filing self-check (AAO denial patterns)

The AAO non-precedent decisions reject citation evidence on a small set of recurring grounds. Confirm the petition addresses each before filing:

- Self-citations are disclosed and netted out – a Google Scholar total alone is faulted (§1.1).
- Evidence is per individual article, not a body-of-work aggregate total (§1.2).
- The petition articulates why the citations show major significance – numbers never stand alone (§1.5).
- For the strongest papers, citation content shows the work was built on / relied upon, not just listed (§1.6, §2.2).
- Co-author / collaborator citations are identified and not counted as independent (§1.7).
- Recognition is shown beyond the scholar's own institution and circle (§1.8).
- Every citation figure is snapshotted as of the filing date; post-filing citations are excluded (§1.9).
- Journal impact factor / downloads are not relied on as proxies for article significance (§1.10, §1.12).
- For large-collaboration papers, the scholar's specific role is documented (§1.13).
- Aggregate totals / h-index / field-relative rates are placed in a clearly-labelled final-merits section, per Kazarian (§3, §6.1.7).

Disclaimer

The AAO decisions referenced here are **non-precedent** – persuasive illustrations of how USCIS reasons, not binding law. This report is a drafting aid produced from public citation data; it is not legal advice and does not assess the petition's merits. All analysis must be reviewed by qualified immigration counsel.

G. Citation Evidence Index

Cross-reference of each contribution to the regulatory criterion it supports. Counsel should map these to the petition's exhibit numbers.

Contribution	Core paper	Indep. cites	Supports
Contribution 1	Production of the Alzheimer amyloid β protein by normal proteolytic processing	8	8 CFR 204.5(h)(3)(v) – Criterion 5
Contribution 2	Age-Dependent Changes in Brain, CSF, and Plasma Amyloid β Protein in the Tg2576 Transgenic Mouse Model of Alzheimer's Disease	8	8 CFR 204.5(h)(3)(v) – Criterion 5
Contribution 3	Cholesterol-dependent γ -secretase activity in buoyant cholesterol-rich membrane microdomains	9	8 CFR 204.5(h)(3)(v) – Criterion 5