

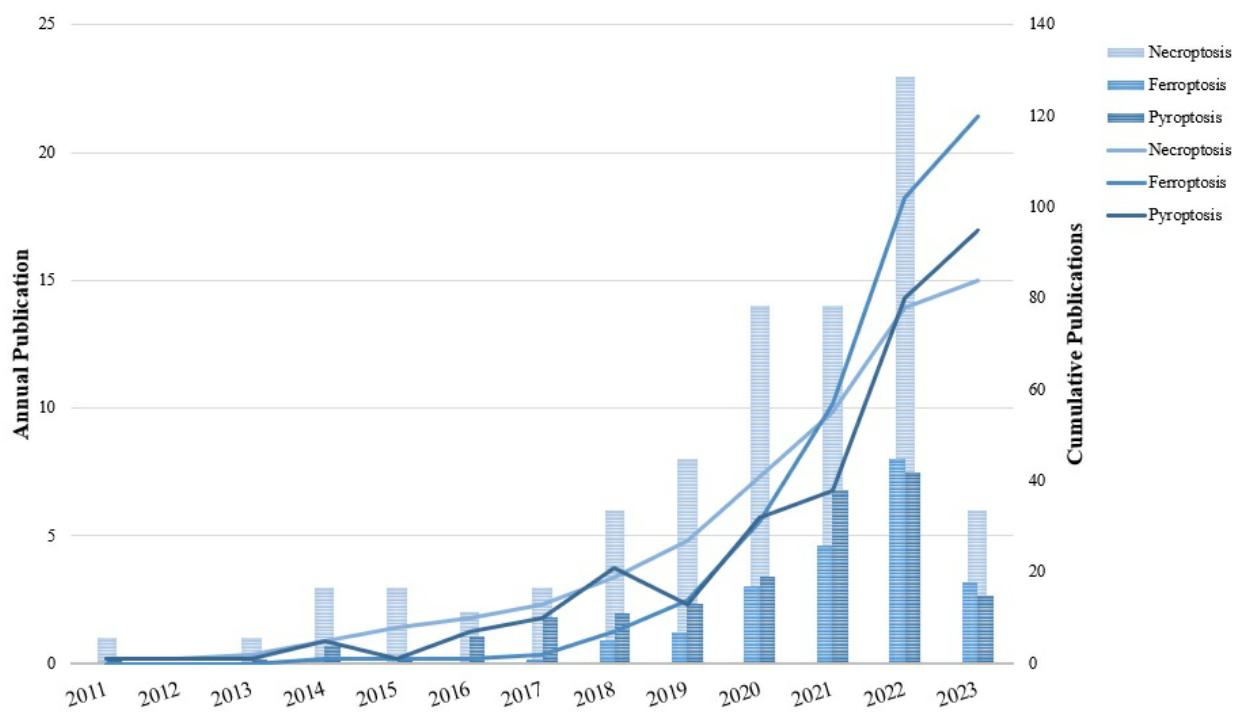
# **Supplementary Material**

## **Global Research Trends and Hotspots for Ferroptosis, Necroptosis, and Pyroptosis in Alzheimer's Disease from the Past to 2023: A Combined Bibliometric Review**

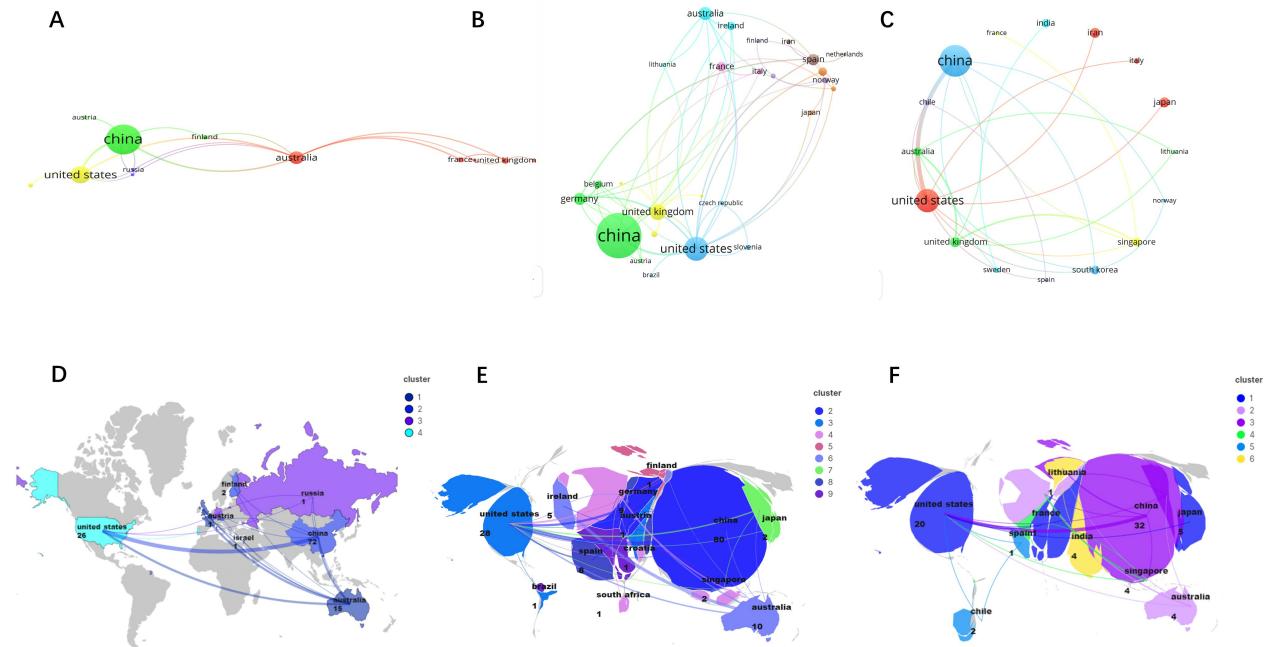
### **Supplementary Material 1**

#1: TS=Alzheimer Dementia OR TS=Alzheimer Dementias OR TS=Dementia, Alzheimer OR TS=Alzheimer's Disease OR TS=Dementia, Senile OR TS=Senile Dementia OR TS=Dementia, Alzheimer Type OR TS=Alzheimer Type Dementia OR TS=Alzheimer-Type Dementia (ATD) OR TS=Alzheimer Type Dementia (ATD) OR TS=Dementia, Alzheimer-Type (ATD) OR TS=Alzheimer Type Senile Dementia OR TS=Primary Senile Degenerative Dementia OR TS=Dementia, Primary Senile Degenerative OR TS=Alzheimer Sclerosis OR TS=Sclerosis, Alzheimer OR TS=Alzheimer Syndrome OR TS=Alzheimer's Diseases OR TS=Alzheimer Diseases OR TS=Alzheimers Diseases OR TS=Senile Dementia, Alzheimer Type OR TS=Acute Confusional Senile Dementia OR TS=Senile Dementia, Acute Confusional OR TS=Dementia, Presenile OR TS=Presenile Dementia OR TS=Alzheimer Disease, Late Onset OR TS=Late Onset Alzheimer Disease OR TS=Alzheimer's Disease, Focal Onset OR TS=Focal Onset Alzheimer's Disease OR TS=Familial Alzheimer Disease (FAD) OR TS=Alzheimer Disease, Familial (FAD) OR TS=Familial Alzheimer Diseases (FAD) OR TS=Alzheimer Disease, Early Onset OR TS=Early Onset Alzheimer Disease OR TS=Presenile Alzheimer Dementia

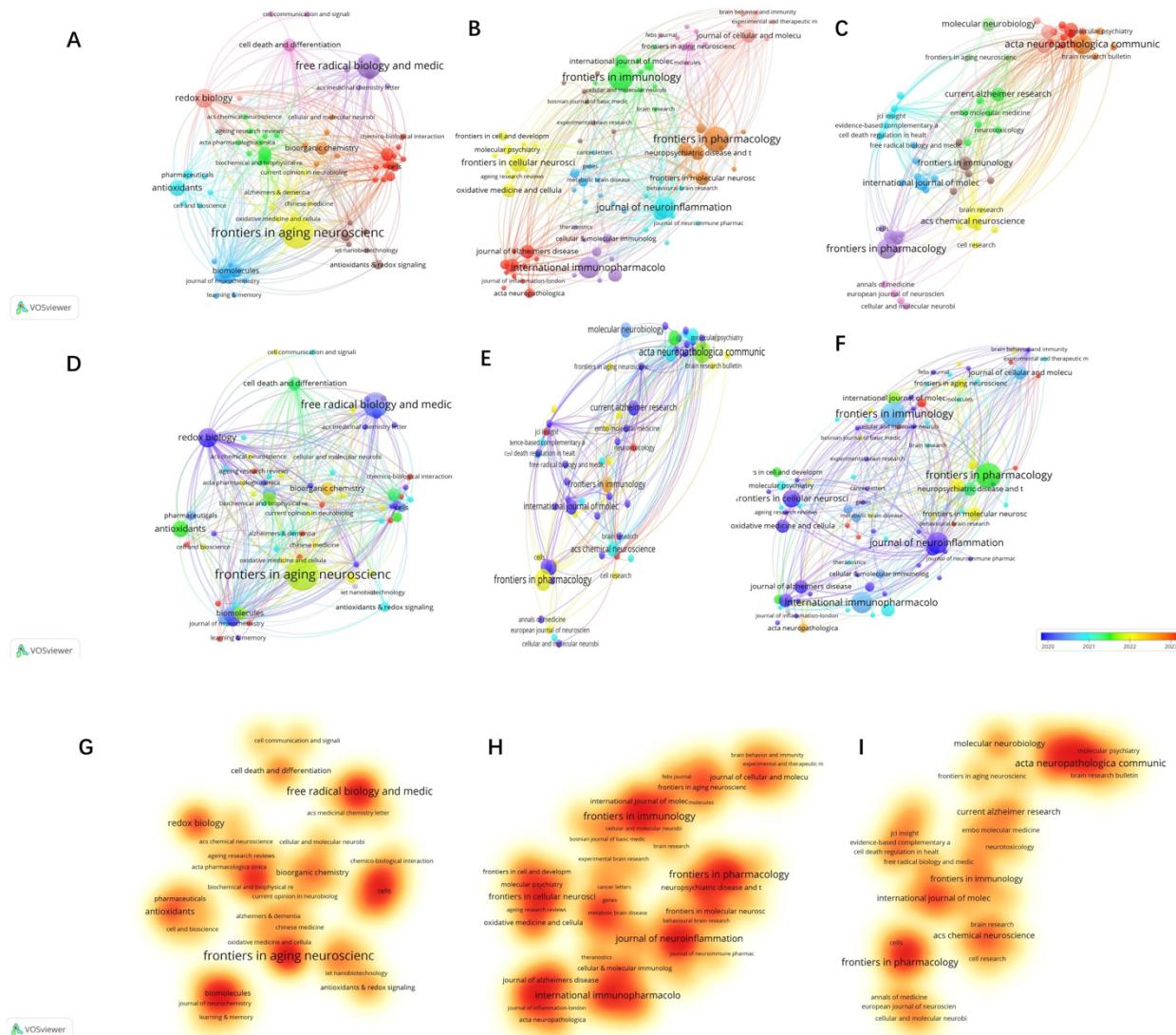
**Supplementary Figure 1.** The number of articles published varied by year.



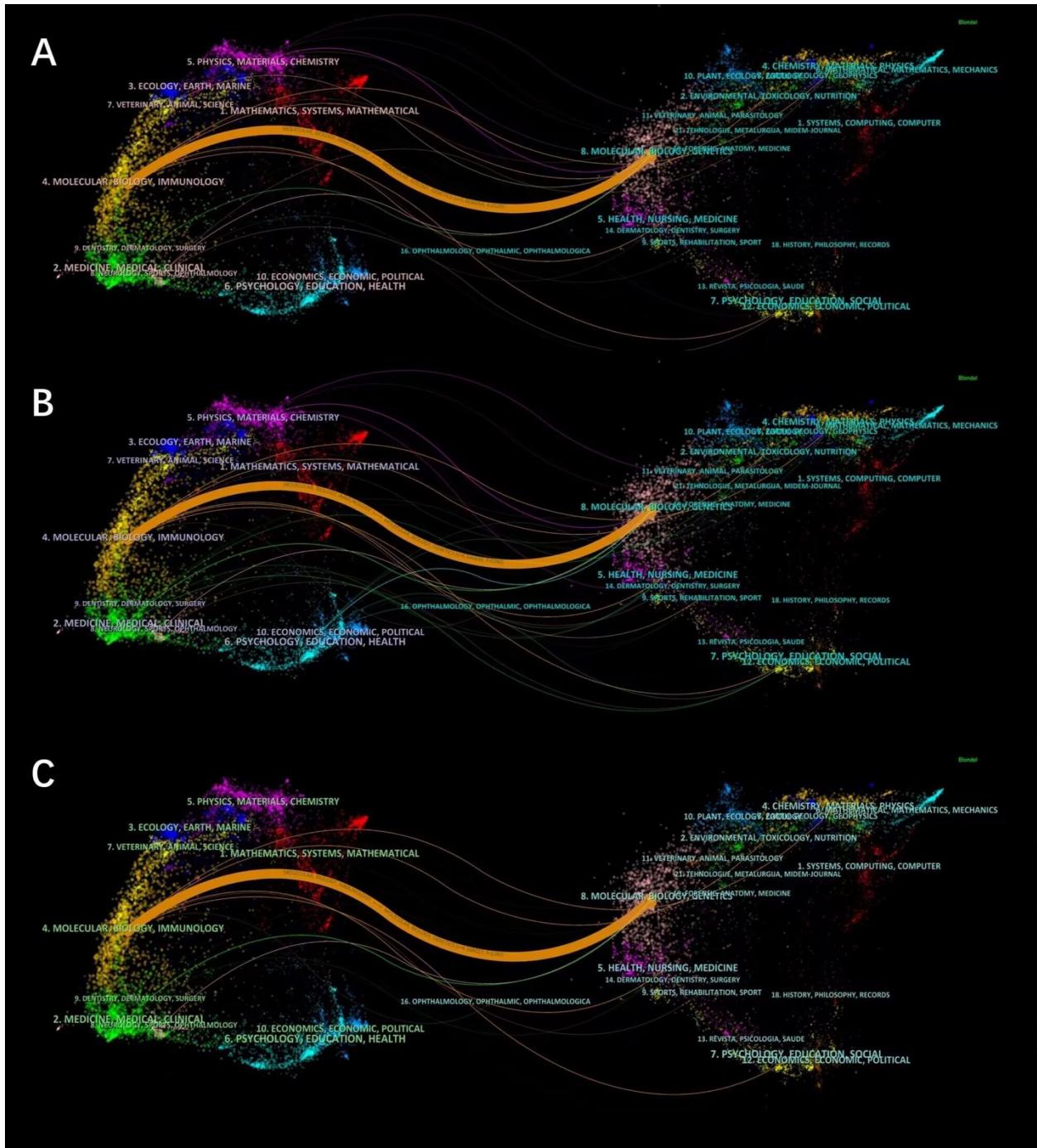
**Supplementary Figure 2.** Visualization of countries related to "ferroptosis in AD" (A), "pyroptosis in AD" (B), and "necroptosis in AD" (C). The size of the nodes corresponds to the number of publications, the lines represent collaboration, and the line thickness represents the intensity of connections. The extent of international cooperation between nations for "ferroptosis in AD" (D), "pyroptosis in AD" (E), and "necroptosis in AD" (F) are shown.



**Supplementary Figure 3.** Visualization of journals related to "ferroptosis in AD" (A), "pyroptosis in AD" (B), and "necroptosis in AD" (C). The number of published articles varied by year published related to "ferroptosis in AD" (D), "pyroptosis in AD" (E), and "necroptosis in AD" (F). The journals' collaborative density maps related to "ferroptosis in AD" (G), "pyroptosis in AD" (H), and "necroptosis in AD" (I).



**Supplementary Figure 4.** The journal double maps of "ferroptosis in AD", "pyroptosis in AD", and "necroptosis in AD".



**Supplementary Table 1.** The top ten authors with the most published articles on Ferroptosis in Alzheimer's disease, Pyroptosis in Alzheimer's disease, and Necroptosis in Alzheimer's disease.

	Rank	Author	Documents	Citations	Average citation/publication
Ferroptosis in AD	1	bush, ashley, i	12	804	67.00
	2	ayton, scott	10	543	54.30
	3	maher, pamela	9	225	25.00
	4	currais, antonio	7	151	21.57
	5	belaidi, abdel ali	5	348	69.60
	6	fan, yong-gang	4	213	53.25
	7	liang, zhibin	4	44	11.00
	8	lane, darius j. r.	3	177	59.00
	9	lei, peng	3	359	119.67
	10	masaldan, shashank	3	294	98.00
Pyroptosis in AD	1	guan, qiaobing	4	140	35.00
	2	guo, li	4	120	30.00
	3	han, chenyang	4	123	30.75
	4	shen, heping	4	140	35.00
	5	sheng, yongjia	4	140	35.00
	6	yang, yi	4	123	30.75
	7	chan, elaine wan ling	3	75	25.00
	8	gan, sook yee	3	75	25.00
	9	genc, sermin	3	28	9.33
	10	gordon, richard	3	403	134.33
Necroptosis in AD	1	yuan, junying	4	577	144.25
	2	koh, rhun-yian	3	45	15.00
	3	niu, qiao	3	60	20.00
	4	thal, dietmar rudolf	3	67	22.33
	5	arunsak, busarin	2	19	9.50
	6	baek, seungyeop	2	104	52.00
	7	balusu, sriram	2	63	31.50
	8	chakrabarti, sasanka	2	20	10.00
	9	chan, hong-hao	2	5	2.50
	10	chattipakorn, nipon	2	19	9.50

**Supplementary Table 2.** The top 10 cited articles of Ferroptosis Alzheimer's disease, Pyroptosis in Alzheimer's disease, and Necroptosis in Alzheimer's disease.

	Rank	Citations	Authors	Title	Source	Year	DOI
Ferroptosis in AD	1	61	Hambright WS	Ablation of ferroptosis regulator glutathione peroxidase 4 in forebrain neurons promotes cognitive impairment and neurodegeneration	Redox Biology	2017	10.1016/j.redox.2017.01.021
	2	52	Stockwell BR	Ferroptosis: A Regulated Cell Death Nexus Linking Metabolism, Redox Biology, and Disease	Cell	2017	10.1016/j.cell.2017.09.021
	3	34	Bao WD	Loss of ferroportin induces memory impairment by promoting ferroptosis in Alzheimer's disease	Cell Death & Differentiation	2021	10.1038/s41418-020-00685-9
	4	33	Ayton S	Brain iron is associated with accelerated cognitive decline in people with Alzheimer pathology	Molecular Psychiatry	2020	10.1038/s41380-019-0375-7
	5	31	Zhang YH	$\alpha$ -Lipoic acid improves abnormal behavior by mitigation of oxidative stress, inflammation, ferroptosis, and tauopathy in P301S Tau transgenic mice	Redox Biology	2018	10.1016/j.redox.2017.11.001
	6	27	Ashraf A	Iron dyshomeostasis, lipid peroxidation and perturbed expression of cystine/glutamate antiporter in Alzheimer's disease: Evidence of ferroptosis	Redox Biology	2020	10.1016/j.redox.2020.101494
	7	26	Doll S	FSP1 is a glutathione-independent ferroptosis suppressor	Nature	2019	10.1038/s41586-019-1707-0
	8	24	Doll S	ACSL4 dictates ferroptosis sensitivity by shaping cellular lipid composition	Nature Chemical Biology	2017	10.1038/NCHEM BIO.2239
	9	22	Yan N	Iron Metabolism, Ferroptosis, and the Links with Alzheimer's Disease	Frontiers in Neuroscience	2020	10.3389/fnins.2019.01443
	10	21	Bersuker K	The CoQ oxidoreductase FSP1 acts parallel to GPX4 to inhibit ferroptosis	Nature	2019	10.1038/s41586-019-1705-2
Pyroptosis in AD	1	29	Ising C	NLRP3 inflammasome activation drives tau pathology	Nature	2019	10.1038/s41586-019-1769-z

	2	25	Dempsey C	Inhibiting the NLRP3 inflammasome with MCC950 promotes non-phlogistic clearance of amyloid- $\beta$ and cognitive function in APP/PS1 mice	Brain, Behavior, and Immunity	2017	10.1016/j.bbi.2016.12.014
	3	22	Han CY	New mechanism of nerve injury in Alzheimer's disease: $\beta$ -amyloid-induced neuronal pyroptosis	Journal of Cellular and Molecular Medicine	2020	10.1111/jcmm.15439
	4	21	Stancu IC	Aggregated Tau activates NLRP3-ASC inflammasome exacerbating exogenously seeded and non-exogenously seeded Tau pathology in vivo	Acta Neuropathologica	2019	10.1007/s00401-018-01957-y
	5	21	Shi JJ	Pyroptosis: Gasdermin-Mediated Programmed Necrotic Cell Death	Trends Biochem Sci	2017	10.1016/j.tibs.2016.10.004
	6	20	Venegas C	Microglia-derived ASC specks cross-seed amyloid- $\beta$ in Alzheimer's disease	Nature	2017	10.1038/nature25158
	7	19	Coll RC	A small-molecule inhibitor of the NLRP3 inflammasome for the treatment of inflammatory diseases	Nature Medicine	2015	10.1038/nm.3806
	8	19	Saresella M	The NLRP3 and NLRP1 inflammasomes are activated in Alzheimer's disease	Molecular Neurodegeneration volume	2016	10.1186/s13024-016-0088-1
	9	19	Gordon R	Inflammasome inhibition prevents $\alpha$ -synuclein pathology and dopaminergic neurodegeneration in mice	Science Translational Medicine	2018	10.1126/scitranslmed.aah4066
	10	19	Heneka MT	NLRP3 is activated in Alzheimer's disease and contributes to pathology in APP/PS1 mice	Nature	2013	10.1038/nature11729
Necroptosis in AD	1	44	Caccamo A	Necroptosis activation in Alzheimer's disease	Nature Neuroscience	2017	10.1038/nn.4608

	2	24	Yuan JY	Necroptosis and RIPK1-mediated neuroinflammation in CNS diseases	Nature Reviews Neuroscience	2019	10.1038/s41583-018-0093-1
	3	24	Ofengheim D	RIPK1 mediates a disease-associated microglial response in Alzheimer's disease	Proceedings of the National Academy of Sciences of USA	2017	10.1073/pnas.1714175114
	4	17	Yang SH	Nec-1 alleviates cognitive impairment with reduction of A $\beta$ and tau abnormalities in APP/PS1 mice	EMBO Mol Med	2017	10.15252/emmm.201606566
	5	16	Koper MJ	Necrosome complex detected in granulovacuolar degeneration is associated with neuronal loss in Alzheimer's disease	Acta Neuropathologica	2020	10.1007/s00401-019-02103-y
	6	16	Ito Y	RIPK1 mediates axonal degeneration by promoting inflammation and necroptosis in ALS	SCIENCE	2016	10.1126/science.aaf6803
	7	14	Iannielli A	Pharmacological Inhibition of Necroptosis Protects from Dopaminergic Neuronal Cell Death in Parkinson's Disease Models	Cell Reports	2018	10.1016/j.celrep.2018.01.089
	8	11	Ofengheim D	Activation of Necroptosis in Multiple Sclerosis	Cell Reports	2015	10.1016/j.celrep.2015.02.051
	9	9	Zhang S	Necroptosis in neurodegenerative diseases: a potential therapeutic target	Cell Death & Disease	2017	10.1038/cddis.2017.286
	10	8	Grootjans S	Initiation and execution mechanisms of necroptosis: an overview	Cell Death & Differentiation	2017	10.1038/cdd.2017.65

**Supplementary Table 3.** The table enumerates the clusters on Ferroptosis Alzheimer's disease, Pyroptosis in Alzheimer's disease, and Necroptosis in Alzheimer's disease.

	ClusterID	Size	Silhouette	Label (LLR)	Average Year
Ferroptosis in AD	0	39	0.907	selective ferroptosis vulnerability	2017
	1	33	0.89	age-associated neurodegenerative diseases	2018
	2	28	0.942	iron exposure	2019
	3	27	0.872	ferroptosis-related biomarker	2018
	4	26	0.997	targeting iron	2016
	5	25	0.997	diverse brain diseases	2014
	6	25	0.903	therapeutic target	2018
	7	22	0.843	brain diseases	2018
	9	18	0.944	potential role	2019
	10	14	0.863	key role	2017
	11	13	0.891	cellular senescence	2017
	12	11	0.92	iron-related newcomer	2016
Pyroptosis in AD	0	59	0.914	pathological tau	2018
	1	58	0.91	regulated cell death	2018
	2	42	0.922	ion fluxe	2014
	3	25	0.971	spatial memory	2016
	5	23	1	nlrp1 inflammasome	2012
	6	23	0.883	brainiac caspases	2016
	7	23	0.874	pharmacological condition	2018
	8	18	0.866	ethanol-induced nlrp3 inflammasome activation	2012
	9	18	0.932	relevant pathological entities	2017
	11	16	0.966	alpha-synuclein pathology	2011
	12	16	0.964	neuronal cell death	2015
	0	35	0.948	ripk1-mediated neuroinflammation	2016
Necroptosis in AD	2	29	0.963	coeloglossum viride var	2018
	3	27	0.904	molecular mechanism	2016

	5	26	0.995	potential role	2015
	6	25	0.872	tnf-mediated neuroinflammation	2018
	8	21	0.995	discovery feature	2017
	10	13	0.966	targeting necroptosis	2019
	12	13	1	necroptosis machinery	2019
	15	10	0.97	potential therapeutic target	2015

**Supplementary Table 4.** The top 10 keywords with the highest frequency and centrality appeared in ferroptosis in Alzheimer's disease, pyroptosis in Alzheimer's disease, and necroptosis in Alzheimer's disease.

	Rank	Freq	Label	Centrality	Label
Ferroptosis in AD	1	72	alzheimers disease	0.4	alpha lipoic acid
	2	67	oxidative stress	0.34	activation
	3	49	lipid peroxidation	0.32	cerebrospinal fluid
	4	43	cell death	0.26	brain iron
	5	32	parkinsons disease	0.23	neurofibrillary tangles
	6	30	glutathione peroxidase 4	0.22	transgenic mouse model
	7	28	cognitive impairment	0.22	cells
	8	20	amyloid precursor protein	0.22	in vivo
	9	19	mouse model	0.21	accumulation
	10	15	amyloid beta	0.2	central nervous system
Pyroptosis in AD	1	102	alzheimers disease	0.43	brain
	2	63	nlrp3 inflammasome	0.35	caspase 1 activation
	3	47	activation	0.25	gasdermin d
	4	33	cell death	0.22	activation
	5	28	amyloid beta	0.22	central nervous system
	6	20	mouse model	0.22	contributes
	7	19	gasdermin d	0.21	cell death
	8	18	expression	0.19	mouse model
	9	18	nalp3 inflammasome	0.18	apoptosis
	10	17	oxidative stress	0.18	age
Necroptosis in AD	1	50	alzheimers disease	0.45	cell death
	2	31	cell death	0.35	alzheimers disease
	3	21	activation	0.34	amyloid precursor protein
	4	15	apoptosis	0.28	apoptosis
	5	15	oxidative stress	0.26	a beta
	6	14	mixed lineage kinase	0.2	brain

	7	11	cognitive impairment	0.19	cognitive impairment
	8	11	amyloid beta	0.17	oxidative stress
	9	9	inflammation	0.15	impairment
	10	9	necroptosis	0.13	activation

**Supplementary Table 5.** The top 10 most productive countries and institutions on Ferroptosis in Alzheimer's disease, Pyroptosis in Alzheimer's disease, and Necroptosis in Alzheimer's disease.

	Rank	Country/region	Documents	Citations	Average citation/publication
Ferroptosis in AD	1	China	72	1666	23.14
	2	United States	26	1397	53.73
	3	Australia	15	1223	81.53
	4	India	4	27	6.75
	5	United Kingdom	4	193	48.25
	6	France	3	311	103.67
	7	Brazil	2	112	56.00
	8	Finland	2	12	6.00
	9	Italy	2	15	7.50
	10	Portugal	2	30	15.00
Pyroptosis in AD	1	China	80	1824	22.80
	2	United States	28	2017	72.04
	3	United Kingdom	14	909	64.93
	4	Australia	10	1488	148.80
	5	Germany	9	920	102.22
	6	Spain	8	761	95.13
	7	France	6	149	24.83
	8	Ireland	5	793	158.60
	9	South Korea	5	150	30.00
	10	Belgium	4	343	85.75
Necroptosis in AD	1	China	32	669	20.91
	2	United States	20	1047	52.35
	3	Iran	5	22	4.40
	4	Japan	5	179	35.80
	5	United Kingdom	5	554	110.80
	6	Australia	4	665	166.25

	7	India	4	45	11.25
	8	Singapore	4	72	18.00
	9	South Korea	4	157	39.25
	10	Belgium	3	67	22.33
	<b>Rank</b>	<b>institutions</b>	<b>Documents</b>	<b>Citations</b>	<b>Average citation/publication</b>
Ferroptosis in AD	1	Univ Melbourne	15	1223	81.53
	2	Salk Inst Biol Studies	9	225	25.00
	3	China Med Univ	5	12	2.40
	4	Cent South Univ	4	3	0.75
	5	HuaZhong Univ Sci & Technol	4	173	43.25
	6	Jilin Univ	4	42	10.50
	7	Sichuan Univ	4	359	89.75
	8	Capital Med Univ	3	251	83.67
	9	Fudan Univ	3	49	16.33
	10	Nanchang univ	3	33	11.00
Pyroptosis in AD	1	NanJing Med Univ	7	436	62.29
	2	JiaXing Univ	6	151	21.57
	3	Univ Queensland	6	819	117.00
	4	QingDao Univ	5	343	49.00
	5	Cent South Univ	4	97	13.86
	6	NanJing Univ	4	118	16.86
	7	Trinity Coll Dublin	4	417	59.57
	8	Univ Manchester	4	190	27.14
	9	Univ Sci & Technol China	4	296	42.29
	10	Dokuz Eylul Univ	3	28	4.00
Necroptosis in AD	1	Shanxi Med Univ	4	71	17.75
	2	Chinese Acad Sci	3	26	8.67
	3	Harvard Med Sch	3	577	192.33

	4	Int Med Univ	3	45	15.00
	5	Katholieke Univ Leuven	3	67	22.33
	6	Korea Inst Sci & Technol	3	135	45.00
	7	NanYang Technol Univ	3	60	20.00
	8	Sun Yat Sen Univ	3	128	42.67
	9	Capital Med Univ	2	20	10.00
	10	Chiang Mai Univ	2	19	9.50

**Supplementary Table 6.** The top 10 most productive journals on Ferroptosis in Alzheimer's disease, Pyroptosis in Alzheimer's disease, and Necroptosis in Alzheimer's disease

	Rank	Source/Journal	Documents	Citations	Average citation/publication	Impact Factor <sup>TM</sup>
Ferroptosis in AD	1	Frontiers in Aging Neuroscience	10	83	8.30	4.8
	2	Free Radical Biology and medicine	7	372	53.14	7.4
	3	Redox Biology	5	799	159.80	11.4
	4	Antioxidants	4	33	8.25	7
	5	Bio Molecules	3	19	6.33	5.5
	6	Bioorganic Chemistry	3	5	1.67	5.1
	7	Cell Death and Differentiation	3	268	89.33	12.4
	8	Frontiers in Cellular Neuroscience	3	11	3.67	5.3
	9	Frontiers in Neuroscience	3	139	46.33	4.3
	10	Frontiers in Pharmacology	3	28	9.33	5.6
Pyroptosis in AD	1	Frontiers in Immunology	6	308	51.33	7.3
	2	Frontiers in Pharmacology	6	64	10.67	5.6
	3	International Immunopharmacology	5	258	51.60	5.6
	4	Journal of Neuroinflammation	5	184	36.80	9.3
	5	Frontiers in Cellular Neuroscience	4	213	53.25	5.3
	6	Cell Death & Disease	3	216	72.00	9
	7	Cells	3	21	7.00	6

	8	Evidence-Based Complementary and Alternative Medicine	3	13	4.33	2.7
	9	Frontiers in Molecular Neuroscience	3	12	4.00	4.8
	10	International Journal of Molecular Sciences	3	28	9.33	5.6
Necroptosis in AD	1	Acta Neuropathologica Communications	3	54	18.00	7.1
	2	Frontiers in Pharmacology	3	35	11.67	5.6
	3	ACS Chemical Neuroscience	2	29	14.50	5
	4	Biomedicine & Pharmacotherapy	2	18	9.00	7.5
	5	Cell Death and Differentiation	2	222	111.00	12.4
	6	CNS & Neurological Disorders-Drug targets	2	25	12.50	3
	7	Current Alzheimer Research	2	22	11.00	2.1
	8	Frontiers in Immunology	2	12	6.00	7.3
	9	Geroscience	2	71	35.50	5.6
	10	International Journal of Molecular Sciences	2	165	82.50	5.6