

## Anti-aging Strategies and Remedies:

### A Landscape of Research Progress and Promise

Rumiana Tenchov, Janet M. Sasso, Xinmei Wang, Qiongqiong Angela Zhou\*

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**Table S1.** Representative anti-aging drugs in the CAS Content Collection

| Anti-aging compounds      | CAS Reg #    | Number of journal articles | Number of patents | ALL  |
|---------------------------|--------------|----------------------------|-------------------|------|
| Acacetin                  | 480-44-4     | 21                         | 12                | 33   |
| Acarbose                  | 56180-94-0   | 87                         | 19                | 106  |
| Acetyl-coenzyme A (Acetyl | 72-89-9      | 147                        | 11                | 158  |
| Acetyl-L-carnitine        | 3040-38-8    | 722                        | 596               | 1318 |
| Acteoside                 | 61276-17-3   | 28                         | 16                | 44   |
| Adapalene                 | 106685-40-9  | 7                          | 52                | 59   |
| Agmatine                  | 306-60-5     | 10                         | 4                 | 14   |
| Allantoin                 | 3040-38-8    | 45                         | 652               | 697  |
| Allicin                   | 539-86-6     | 23                         | 46                | 69   |
| Aloesin                   | 30861-27-9   | 2                          | 16                | 18   |
| Anacardic acid            | 11034-77-8   | 3                          | 8                 | 11   |
| Andrographolide           | 5508-58-7    | 17                         | 15                | 32   |
| Antcin M                  | 1005344-44-4 | 1                          | 2                 | 3    |
| Apigenin                  | 520-36-5     | 132                        | 102               | 234  |
| Arginine, L-              | 74-79-3      | 726                        | 615               | 1341 |
| Aspirin                   | 50-78-2      | 3569                       | 162               | 3731 |
| Astaxanthin               | 472-61-7     | 136                        | 436               | 572  |
| Astragaloside             | 17429-69-5   | 27                         | 31                | 58   |
| Azacitidine               | 320-67-2     | 47                         | 21                | 68   |
| AZD8055                   | 1009298-09-2 | 3                          | 4                 | 7    |
| Bacoside A                | 11028-00-5   | 3                          | 0                 | 3    |
| Baicalein                 | 491-67-8     | 41                         | 37                | 78   |
| Berberine                 | 2086-83-1    | 80                         | 34                | 114  |
| Betaine                   | 107-43-7     | 113                        | 571               | 684  |
| Betulinic acid            | 472-15-1     | 30                         | 49                | 79   |
| Butein                    | 487-52-5     | 10                         | 19                | 29   |
| Caffeic acid              | 331-39-5     | 226                        | 129               | 355  |
| Carnosic acid             | 3650-09-7    | 22                         | 36                | 58   |
| Carnosine, L-             | 305-84-0     | 177                        | 379               | 556  |
| β-Carotene                | 7235-40-7    | 687                        | 327               | 1014 |
| Catalpol                  | 2415-24-9    | 20                         | 6                 | 26   |
| Catechin                  | 154-23-4     | 512                        | 288               | 800  |
| Celastrol                 | 34157-83-0   | 13                         | 7                 | 20   |
| Chicoric acid             | 6537-80-0    | 8                          | 11                | 19   |
| Chlorogenic acid          | 327-97-9     | 221                        | 122               | 343  |
| Chromium picolinate       | 14639-25-9   | 10                         | 18                | 28   |
| Chrysin                   | 480-40-0     | 32                         | 39                | 71   |

|                                  |              |     |      |      |
|----------------------------------|--------------|-----|------|------|
| Chrysophanol                     | 481-74-3     | 8   | 8    | 16   |
| Coenzyme Q10                     | 303-98-0     | 242 | 541  | 783  |
| Crocin                           | 42553-65-1   | 228 | 64   | 292  |
| Curculigoside                    | 85643-19-2   | 5   | 1    | 6    |
| Curcumin                         | 458-37-7     | 444 | 210  | 654  |
| Cycloastragenol (Telomera        | 78574-94-4   | 35  | 18   | 53   |
| Danazol                          | 17230-88-5   | 15  | 5    | 20   |
| Dapagliflozin (Dapagliflozo      | 461432-26-8  | 45  | 9    | 54   |
| Dasatinib                        | 302962-49-8  | 39  | 21   | 60   |
| Dehydroabietic acid              | 1740-19-8    | 6   | 7    | 13   |
| Dehydroepiandrosterone (         | 53-43-0      | 388 | 132  | 520  |
| 2-Deoxy-D-glucose                | 154-17-6     | 83  | 14   | 97   |
| Elamipretide                     | 736992-21-5  | 4   | 7    | 11   |
| Ellagic acid                     | 476-66-4     | 115 | 156  | 271  |
| Emodin                           | 518-82-1     | 39  | 18   | 57   |
| Entinostat (SNDX-275; MS-        | 209783-80-2  | 3   | 11   | 14   |
| (-)-Epicatechin                  | 490-46-0     | 202 | 119  | 321  |
| Epigallocatechin-3-gallate       | 989-51-5     | 292 | 180  | 472  |
| Epitalon                         | 307297-39-8  | 31  | 1    | 32   |
| Ergoloid mesylate (Hyderg        | 8067-24-1    | 6   | 2    | 8    |
| 17- $\alpha$ -Estradiol          | 57-91-0      | 24  | 3    | 27   |
| Ethanolamine                     | 141-43-5     | 40  | 132  | 172  |
| Ferulic acid                     | 1135-24-6    | 184 | 248  | 432  |
| Fisetin                          | 528-48-3     | 59  | 47   | 106  |
| Fucoxanthin                      | 3351-86-8    | 23  | 27   | 50   |
| Galangin                         | 548-83-4     | 16  | 11   | 27   |
| Gallic acid                      | 149-91-7     | 345 | 144  | 489  |
| Garcinol                         | 78824-30-3   | 4   | 1    | 5    |
| Garlicin                         | 2179-57-9    | 10  | 19   | 29   |
| Gastrodin                        | 62499-27-8   | 16  | 8    | 24   |
| Genistein                        | 446-72-0     | 216 | 150  | 366  |
| Gingerol                         | 58253-27-3   | 14  | 15   | 29   |
| [6]-Gingerol                     | 23513-14-6   | 9   | 9    | 18   |
| Ginsenoside Rg1                  | 22427-39-0   | 98  | 30   | 128  |
| Glabridin                        | 59870-68-7   | 9   | 85   | 94   |
| Glaucarubinone                   | 1259-86-5    | 2   | 1    | 3    |
| Glipizide                        | 29094-61-9   | 14  | 16   | 30   |
| $\beta$ -Guanidinopropionic acid | 353-09-3     | 4   | 0    | 4    |
| Glucosamine, D-                  | 3416-24-8    | 121 | 190  | 311  |
| HDTIC-1                          | 1229519-12-3 | 2   | 0    | 2    |
| HDTIC-2                          | 1229519-13-4 | 2   | 0    | 2    |
| Hesperidin                       | 520-26-3     | 72  | 99   | 171  |
| Honokiol                         | 35354-74-6   | 19  | 31   | 50   |
| Human growth hormone (I          | 12629-01-5   | 200 | 18   | 218  |
| Huperzine A                      | 102518-79-6  | 10  | 6    | 16   |
| Hyaluronic acid                  | 9004-61-9    | 584 | 2081 | 2665 |

|                            |             |     |     |      |
|----------------------------|-------------|-----|-----|------|
| Hydroxycitric acid (HCA)   | 27750-10-3  | 8   | 10  | 18   |
| 4-Hydroxy phenyl N-tert-b  | 223649-80-7 | 2   | 2   | 4    |
| Icariin                    | 489-32-7    | 38  | 14  | 52   |
| Idebenone                  | 58186-27-9  | 15  | 49  | 64   |
| Isotretinoin               | 4759-48-2   | 60  | 61  | 121  |
| Kaempferol                 | 520-18-3    | 204 | 111 | 315  |
| $\alpha$ -Ketoglutarate    | 328-50-7    | 81  | 31  | 112  |
| Lactic acid                | 50-21-5     | 414 | 555 | 969  |
| Lauric acid                | 143-07-7    | 92  | 236 | 328  |
| $\alpha$ -Lipoic acid      | 1200-22-2   | 209 | 346 | 555  |
| Liquiritin                 | 551-15-5    | 11  | 17  | 28   |
| Lithium                    | 7439-93-2   | 266 | 145 | 411  |
| Lutein                     | 127-40-2    | 385 | 189 | 574  |
| Luteolin                   | 491-70-3    | 146 | 100 | 246  |
| Mangiferin                 | 4773-96-0   | 16  | 15  | 31   |
| Meclofenoxate (Centroph    | 51-68-3     | 34  | 9   | 43   |
| Melatonin                  | 73-31-4     | 637 | 176 | 813  |
| Metformin                  | 657-24-9    | 936 | 105 | 1041 |
| Methylthiomethane (Dime    | 75-18-3     | 4   | 10  | 14   |
| Mogroside                  | 872869-50-6 | 3   | 9   | 12   |
| Monascin                   | 21516-68-7  | 4   | 0   | 4    |
| Myricetin                  | 529-44-2    | 87  | 60  | 147  |
| N-Acetylcysteine           | 7218-04-4   | 48  | 9   | 57   |
| Naringenin                 | 480-41-1    | 88  | 63  | 151  |
| Nicotinamide               | 98-92-0     | 575 | 884 | 1459 |
| Nicotinamide riboside      | 1341-23-7   | 62  | 41  | 103  |
| Nordihydroguaiaretic acid  | 500-38-9    | 28  | 46  | 74   |
| Oleanolic acid             | 508-02-1    | 77  | 69  | 146  |
| Oleuropein                 | 32619-42-4  | 60  | 40  | 100  |
| Oligonol                   | 851983-55-6 | 6   | 3   | 9    |
| Orientin                   | 28608-75-5  | 18  | 10  | 28   |
| Oxymatrine                 | 16837-52-8  | 4   | 3   | 7    |
| Panobinostat               | 404950-80-7 | 5   | 9   | 14   |
| Pegvisomant                | 218620-50-9 | 3   | 4   | 7    |
| Phosphatidylserine         | -           | 208 | 84  | 292  |
| Phycocyanin C              | 11016-15-2  | 24  | 23  | 47   |
| Piracetam                  | 7491-74-9   | 43  | 10  | 53   |
| Polydatin (Piceid)         | 27208-80-6  | 26  | 29  | 55   |
| Procaine (Gerovital H3, GI | 59-46-1     | 60  | 35  | 95   |
| Procyanidin B3             | 3567-23-9   | 1   | 2   | 3    |
| Protandim                  | 877143-83-4 | 3   | 0   | 3    |
| Protocatechuic aldehyde    | 139-85-5    | 15  | 25  | 40   |
| Pterostilbene              | 537-42-8    | 47  | 40  | 87   |
| Puerarin                   | 3681-99-0   | 32  | 25  | 57   |
| Pyridopyrimidines          | -           | 1   | 0   | 1    |
| Quercetin                  | 117-39-5    | 654 | 303 | 957  |
| Quercetin caprylate        | 87798-94-5  | 3   | 2   | 5    |

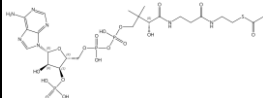
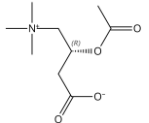
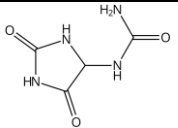
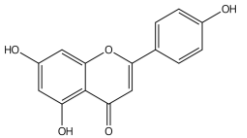
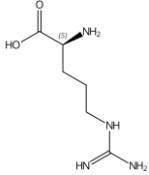
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|-----------------------------------|-------------|------|------|------|
| Rapamycin (Sirolimus)             | 53123-88-9  | 1411 | 99   | 1510 |
| Resveratrol                       | 501-36-0    | 1270 | 602  | 1872 |
| Rosiglitazone                     | 122320-73-4 | 57   | 30   | 87   |
| Rosmarinic acid                   | 20283-92-5  | 83   | 69   | 152  |
| Rutin                             | 153-18-4    | 245  | 183  | 428  |
| Ruxolitinib                       | 941678-49-5 | 23   | 8    | 31   |
| Salicylic acid                    | 69-72-7     | 201  | 711  | 912  |
| Salsalate                         | 552-94-3    | 4    | 13   | 17   |
| Sappanone A                       | 112458-02-3 | 1    | 1    | 2    |
| Selegiline (L-deprenyl, Eldepryl) | 14611-51-9  | 109  | 28   | 137  |
| Seletinoid G                      | 637357-50-7 | 4    | 2    | 6    |
| Sesamin                           | 1143-70-0   | 27   | 17   | 44   |
| Silymarin                         | 65666-07-1  | 43   | 55   | 98   |
| Sirtuin                           | 438496-81-2 | 2235 | 180  | 2415 |
| Sodium butyrate                   | 156-54-7    | 37   | 17   | 54   |
| Sodium phenylbutyrate (Bimastat)  | 1716-12-7   | 7    | 8    | 15   |
| Spermidine                        | 124-20-9    | 235  | 52   | 287  |
| Sulforaphane                      | 4478-93-7   | 73   | 27   | 100  |
| Tadalafil                         | 171596-29-5 | 7    | 11   | 18   |
| Tambulin                          | 571-72-2    | 2    | 0    | 2    |
| Tazarotene                        | 118292-40-3 | 7    | 34   | 41   |
| Tectorigenin                      | 548-77-6    | 3    | 6    | 9    |
| Tetrahydrocurcumin                | 36062-04-1  | 24   | 37   | 61   |
| Theaflavin                        | 4670-05-7   | 26   | 14   | 40   |
| Theanine                          | 3081-61-6   | 32   | 52   | 84   |
| Tiliroside                        | 20316-62-5  | 7    | 5    | 12   |
| Trametinib                        | 871700-17-3 | 7    | 4    | 11   |
| Tretinoin                         | 302-79-4    | 229  | 319  | 548  |
| Trichostatin A                    | 58880-19-6  | 28   | 4    | 32   |
| Tyrosol                           | 501-94-0    | 45   | 16   | 61   |
| Urolithin A                       | 1143-70-0   | 37   | 12   | 49   |
| Ursolic acid                      | 77-52-1     | 69   | 91   | 160  |
| Valproic acid                     | 99-66-1     | 148  | 23   | 171  |
| Vinpocetine                       | 42971-09-5  | 10   | 8    | 18   |
| Visomitin                         | 934826-68-3 | 13   | 3    | 16   |
| Vitamin A (Retinol)               | 68-26-8     | 1141 | 934  | 2075 |
| Vitamin C (L-ascorbic acid)       | 50-81-7     | 2030 | 2482 | 4512 |
| Vitamin E                         | 1406-18-4   | 1593 | 1879 | 3472 |
| Vitexin                           | 3681-93-4   | 29   | 16   | 45   |
| Vorinostat                        | 149647-78-9 | 22   | 21   | 43   |

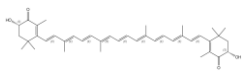
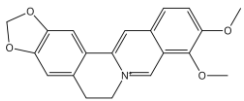
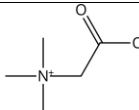
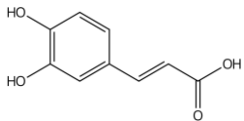
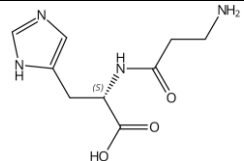
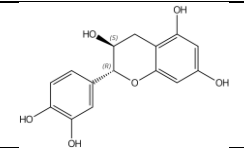
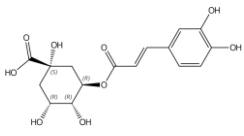
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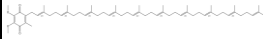
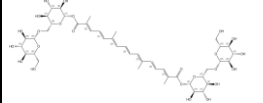
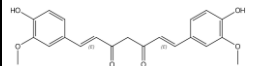
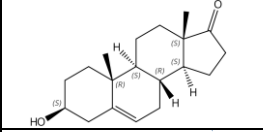
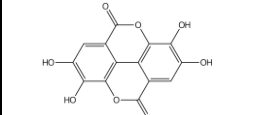
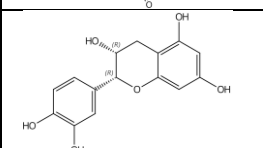
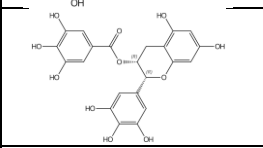
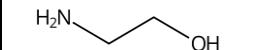
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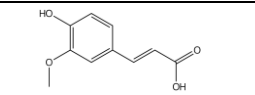
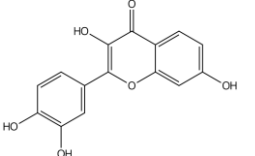
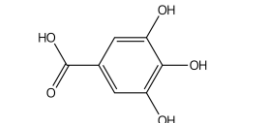
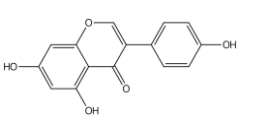
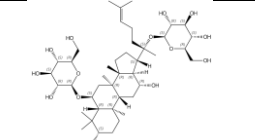
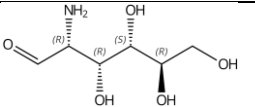
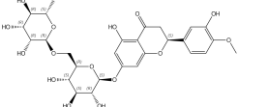
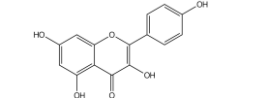
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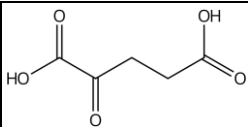
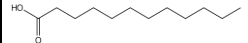
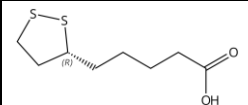
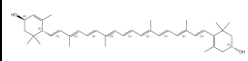
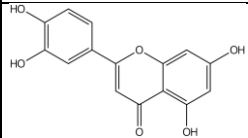
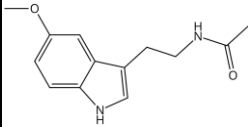
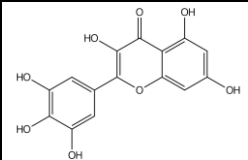
**Table S2.** Natural anti-aging agents most widely represented in the CAS Content Collection including structures <sup>1-18</sup>

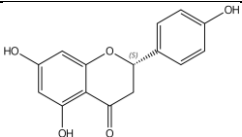
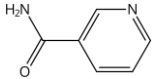
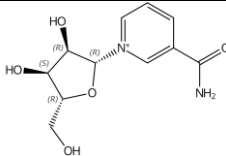
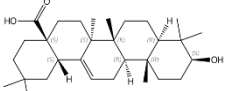
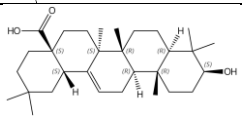
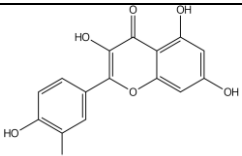
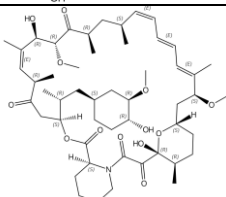
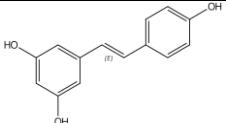
| Natural anti-aging compounds   | CAS REG # | Sources                                                | Mechanism of action / Anti-aging strategy                                                                                         | Application / Benefits                                                                        | Structure                                                                             | Number of journal articles | Number of patents |
|--------------------------------|-----------|--------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------|----------------------------|-------------------|
| Acetyl-coenzyme A (Acetyl CoA) | 72-89-9   | Oily fish (salmon, tuna), organ meat (liver), grains   | Inhibits oxidation of proteins, lipids, and DNA                                                                                   | heart conditions, muscular dystrophy                                                          |    | 147                        | 11                |
| Acetyl-L-carnitine             | 3040-38-8 | Red meat, poultry, fish, dairy foods                   | Decline in interfibrillar mitochondria carnitine palmitoyltransferase 1 activity                                                  | Improves cognitive and neurological function, reduces mental fatigue, improve mood, alertness |    | 722                        | 596               |
| Allantoin                      | 97-59-6   | Chamomile, wheat sprouts, sugar beet, comfrey          | Helps in shedding of dead skin cells & cell turnover                                                                              | Skin moisturizing and soothing, exfoliation, wound healing                                    |   | 45                         | 652               |
| Apigenin                       | 520-36-5  | Chamomile, celeriac, parsley                           | Inhibits skin inflammation by down-regulating transcription factors including AP-1, NF-κB, STAT; CD38 inhibitor                   | Antidiabetic, chemoprevention                                                                 |  | 132                        | 102               |
| Arginine, L-                   | 74-79-3   | Meat, fish, nuts & seeds, legumes, whole grains, dairy | Reduces oxidative stress and inflammation resulting in decreased NF-κB level and activity; vascular smooth muscle cell relaxation | Reduces systolic and diastolic blood pressure in hypertensive patients                        |  | 726                        | 615               |

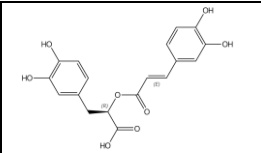
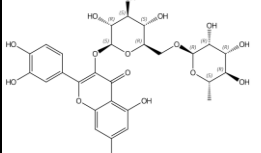
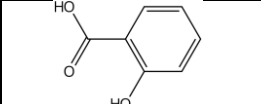
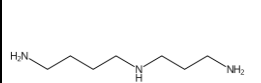
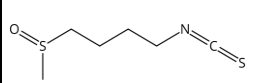
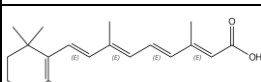
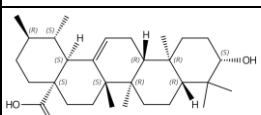
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| Astaxanthin      | 472-61-7  | Phaffia Rhodozyma                                            | Protects cell membranes against reactive oxygen and nitrogen species and oxidative damage                                                                | Antioxidant, anti-inflammatory                                                                                             |    | 136 | 436 |
| Berberine        | 2086-83-1 | Coptidis rhizome, Barberry plants, Chinese goldthread        | AMPK activator, enhancing UCP2 expression, inhibits oxidative stress                                                                                     | Agent against dyslipidemia, antidiabetic, antioxidant, antiobesity, antiangiogenic                                         |    | 80  | 34  |
| Betaine          | 107-43-7  | Sugar beets                                                  | Lowers levels of homocysteine in circulating blood                                                                                                       | Osmoregulator, ergogenic, supporting heart health                                                                          |    | 113 | 571 |
| Caffeic acid     | 331-39-5  | Coffee, red wine, berries, apples, olives, artichokes, pears | Regulates proteostasis; alleviates neuroinflammation and neurodegeneration                                                                               | Antioxidant; liver damage prevention, cognitive function improvement; psychoactive drug                                    |    | 226 | 129 |
| L-Carnosine      | 305-84-0  | Meats: turkey, chicken, beef, pork                           | Reacts with methyl-glyoxal and scavenges ROS thus protective toward aging and ischemia; increase verbal episodic memory; increase of cerebral blood flow | Anti-aging, antioxidant                                                                                                    |    | 177 | 379 |
| β-Carotene       | 7235-40-7 | Fungi, plants, fruits                                        | Photoprotecting agent, reduces rate of mitochondrial mutation                                                                                            | Antioxidant agent, promotes healthy skin, supports immune system, eye health and vision                                    |    | 687 | 327 |
| Catechin         | 154-23-4  | Tea polyphenols                                              | Rich in oligomeric proanthocyanidins, thus prevents premature aging                                                                                      | Anti-inflammatory agent                                                                                                    |  | 512 | 288 |
| Chlorogenic acid | 327-97-9  | Coffee, tea, bamboo                                          | Glucose regulation; induce continuous phosphorylation of ERK1/2                                                                                          | Antioxidant, neuroprotective, anti-inflammatory, gastro-protective, antirheumatic, antihypertensive, anti-atherothrombotic |  | 221 | 122 |

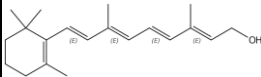
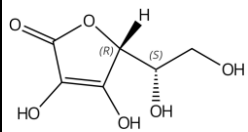
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| Coenzyme Q10                      | 303-98-0   | Meat, fish, nuts                                     | Increases production of key antioxidants such as superoxide dismutase; reduces levels of lipid peroxidation; intensify blood flow, protect blood vessels by upholding nitric oxide                             | Anti-inflammatory, anti-atherogenic                                                                       |    | 242 | 541 |
| Crocin                            | 42553-65-1 | Flowers of crocus and gardenia, saffron              | Reduces oxidative stress and ROS through enhancement of gene expression of Nrf2, HO-1, and antioxidant enzymes CAT, GSH, and SOD; counteract oxidative stress, mitochondrial dysfunction and neuroinflammation | Degenerative disease, metabolic syndrome; antioxidant, neuroprotective agent                              |    | 228 | 64  |
| Curcumin                          | 458-37-7   | Curcuma longa, turmeric                              | Inhibits TOR pathway; autophagy inducing                                                                                                                                                                       | Anti-inflammatory, antioxidant                                                                            |    | 444 | 210 |
| Dehydroepiandrosterone (DHEA)     | 53-43-0    | Wild yam, soy                                        | Activates PPARα and constitutive androstane receptor (CAR)                                                                                                                                                     | Raises androgen and estrogen levels; improves bone & cardiovascular health, insulin sensitivity, and mood |    | 388 | 132 |
| Ellagic acid                      | 476-66-4   | Fruits: grapes, strawberries, pomegranate            | Decreases amount of inflammatory cytokines, regulates the activities of antioxidant enzymes                                                                                                                    | Anti-inflammatory, antioxidant; treats viral and bacterial infections                                     |    | 115 | 156 |
| (-)-Epicatechin                   | 490-46-0   | Cocoa                                                | Stimulates mitochondrial respiration and biogenesis                                                                                                                                                            | Enhances nitric oxide production for improved vascularity, circulation, and resilience                    |   | 202 | 119 |
| Epigallocatechin-3-gallate (EGCG) | 989-51-5   | Green tea                                            | Regulates cytokine secretion, autophagy inducing                                                                                                                                                               | Antioxidant, anti-inflammatory                                                                            |  | 292 | 180 |
| Ethanolamine                      | 141-43-5   | Daikon radish, caraway, muscadine grape, lemon grass | Increases amount of cellular phosphatidylethanolamine, thus stimulating cytoprotective autophagy and anti-aging protection                                                                                     | Anti-aging, inducing autophagy                                                                            |  | 40  | 132 |

|                 |            |                                                        |                                                                                                                                |                                                                                                       |                                                                                       |     |      |
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| Ferulic acid    | 1135-24-6  | Beet roots, oranges, carrots                           | Restrains radiation-induced oxidative stress by ceasing free radical chain reaction                                            | Anti-aging, anticancer                                                                                |    | 184 | 248  |
| Fisetin         | 528-48-3   | Nuts, strawberries, apples, mangoes, persimmons        | Inhibits NF-κB activation, promotes Nrf2 activity to prevent neurodegeneration; lipoxygenase inhibitor                         | Neuroprotective agent; anti-aging, anticancer, anti-inflammatory                                      |    | 59  | 47   |
| Gallic acid     | 149-91-7   | Rose flower                                            | Anti-inflammatory mechanisms involve MAPK and NF-κB signaling pathways; reducing release of inflammatory cytokines, chemokines | Improves cognitive function, motor function; anti-inflammatory                                        |    | 345 | 144  |
| Genistein       | 446-72-0   | Soy products                                           | Enhancing skin collagen by stimulating subcutaneous VEGF expression and increasing TGF-β in skin                               | Maintains arterial elasticity, blood glucose control, prevents hypertension, prostate & breast cancer |    | 216 | 150  |
| Ginsenoside Rg1 | 22427-39-0 | Ginseng                                                | Improves cognitive function; stimulates glucose uptake, relieves oxidative stress; possible neuroprotective role               | Suppressive effects in neurodegenerative conditions; neuroprotectant, anti-inflammatory               |    | 98  | 30   |
| D-Glucosamine   | 3416-24-8  | Chitin from hard outer shells of shrimp, lobster, crab | Prevents collagen degeneration in chondrocytes; slow cartilage deterioration in the joints                                     | Cartilage-protecting, anti-inflammatory                                                               |    | 121 | 190  |
| Hesperidin      | 520-26-3   | Citrus genus                                           | Inhibition of signaling pathway related to MMP-9 activated by UVB radiation                                                    | Antioxidant, anti-inflammatory, anti-aging                                                            |   | 72  | 99   |
| Hyaluronic acid | 9004-61-9  | Rooster combs (the red part on a rooster's neck)       | Major component of extracellular matrix, key role in tissue regeneration, inflammation, angiogenesis, wound repair             | Reduces facial skin wrinkles                                                                          | N/A                                                                                   | 584 | 2081 |
| Kaempferol      | 520-18-3   | Spinach, kale, tarragon                                | Prevents the activation of p38 mitogen-activated protein kinase C-JNK                                                          | Antiapoptotic, antiangiogenic                                                                         |  | 204 | 111  |

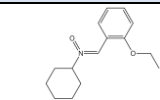
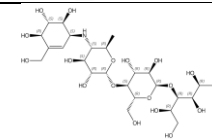
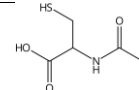
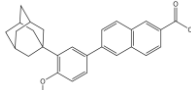
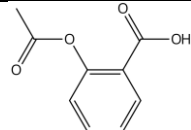
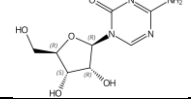
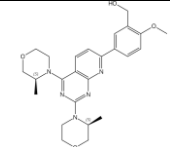
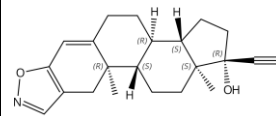
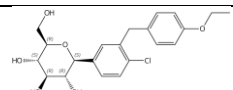
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| $\alpha$ -Ketoglutarate | 328-50-7  | Intermediate of the tricarboxylic acid cycle                                                        | Nitrogen scavenger, glutamate and glutamine source, promotes protein synthesis, prevents protein degradation in muscles                                            | Improves amino acid metabolism                                                                                                               |    | 81  | 31  |
| Lactic acid             | 50-21-5   | Pickled vegetables, yogurt                                                                          | Stimulates collagen renewal                                                                                                                                        | Skin moisturizing and antiwrinkle properties                                                                                                 |    | 414 | 555 |
| Lauric acid             | 143-07-7  | Papaya                                                                                              | Rich in saturated fatty acids, hydrates skin                                                                                                                       | Anti-aging, antimicrobial, anti-bronchitis; soothes inflamed skin, inhibits acne bacteria                                                    |    | 92  | 236 |
| $\alpha$ -Lipoic acid   | 1200-22-2 | Spinach, broccoli, potatoes, yeast, tomatoes, carrots                                               | Suppression of p38 and p53 at gene level                                                                                                                           | Antioxidant, anti-aging                                                                                                                      |    | 209 | 346 |
| Lithium                 | 7439-93-2 | Ore mining, salt water from underground lakes                                                       | Modulates the release of dopamine or serotonin in brain                                                                                                            | Mood stabilizer, helps to treat bipolar episodes                                                                                             | Li                                                                                    | 266 | 145 |
| Lutein                  | 127-40-2  | Green vegetables                                                                                    | Preserves visual function by preventing degradation of rhodopsin and synaptophysin                                                                                 | Prevents skin aging, age-related macular degeneration; antioxidant                                                                           |    | 385 | 189 |
| Luteolin                | 491-70-3  | Vegetables, tea                                                                                     | Reduces neuroinflammation and improves learning and memory; inhibits vascular inflammation                                                                         | Anti-inflammatory, antioxidant                                                                                                               |    | 146 | 100 |
| Melatonin               | 73-31-4   | Tart cherries, tomatoes, corn, asparagus, olives, pomegranate, nuts, sunflower, mustard, flax seeds | Restores mitochondrial membrane permeability, promotes antioxidant enzymes including glutathione peroxidase, superoxide dismutase, glutathione reductase, catalase | Antioxidant, anti-inflammatory, autophagy inducing, anti-aging                                                                               |   | 637 | 176 |
| Myricetin               | 529-44-2  | Berries, red wine                                                                                   | Reduces epidermal thickening provoked by UVB and suppress MMP-9 protein expression and enzyme activity                                                             | Anti-aging; inhibits hyperglycemia, decreases hepatic triglyceride, reduces oxidative stress and cholesterol contents, protects liver injury |  | 87  | 60  |

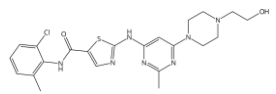
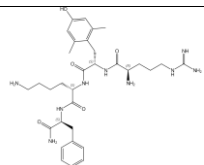
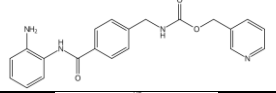
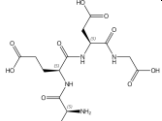
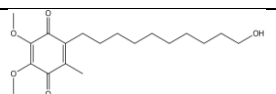
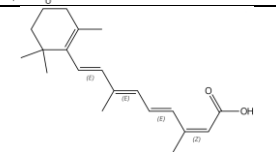
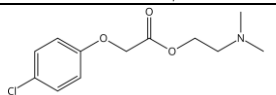
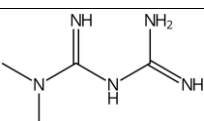
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| Naringenin            | 480-41-1     | Grapefruit, bergamot, orange, cherries, tomatoes, cocoa, oregano, mint                 | Enhances antioxidant ability by activating Nrf2 causing HO-1 expression; inhibit NF-κB activation in macrophages                 | Anti-inflammatory, antioxidant                                                   |    | 88   | 63  |
| Nicotinamide          | 98-92-0      | Meat, milk, eggs, green vegetables                                                     | DAC activator of SIRT1; manages the NF-κB-mediated transcription and inhibits mast cells degranulation; calorie mimetic          | Cell proliferation and improvement in skin texture                               |    | 575  | 884 |
| Nicotinamide riboside | 1341-23-7    | Cow's milk                                                                             | Improves glucose tolerance, reduces age-related weight gain, exhibits neuroprotective effects                                    | Anti-aging; neuroprotection and vascular protection                              |    | 62   | 41  |
| Oleanolic acid        | 508-02-1     | Olea europaea, Viscum album, Aralia chinensis                                          | Regulates macrophage polarization in adipose tissue                                                                              | Antioxidant, anti-inflammatory, antiviral, anti-obesity, antidiabetic            |    | 77   | 69  |
| Oleuropein            | 32619-42-4   | Olives                                                                                 | Avoids the reduction of proteasome activities upon senescence                                                                    | Antiatherogenic, antioxidant, anticancer                                         |    | 60   | 40  |
| Phosphatidylserine    | 1446756-47-3 | Soybeans, egg yolks, liver                                                             | Restores acetylcholine release, increases endogenous choline for de novo acetylcholine synthesis                                 | Antioxidant; reduces stress, anxiety, and depression                             | N/A                                                                                   | 208  | 84  |
| Quercetin             | 117-39-5     | Apples, honey, raspberries, onion, red grape, cherries, citrus, green leafy vegetables | Prevents the production of tumor necrosis factor α in macrophages and IL-8 in lung A549 cells, as induced by lipopolysaccharides | Calorie mimetics, anti-inflammatory, anti-atherogenic                            |   | 654  | 303 |
| Rapamycin (Sirolimus) | 53123-88-9   | Soil bacterium: Streptomyces hygroscopicus                                             | mTORC1 inhibitor; autophagy inducing, dietary restriction, calorie mimetic                                                       | Natural anti-fungal antibiotic                                                   |  | 1411 | 99  |
| Resveratrol           | 501-36-0     | Grapes, berries, Polygonum cuspidatum                                                  | Sirtuin activator; calorie mimetics; telomerase activation                                                                       | Neuroprotective, cardio-protective; antioxidant, anti-inflammatory, antidiabetic |  | 1270 | 602 |

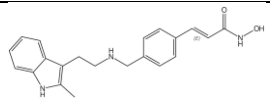
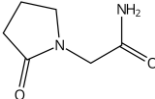
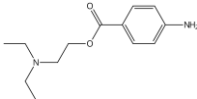
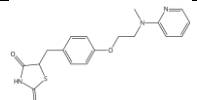
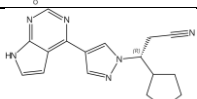
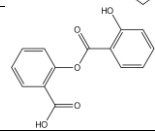
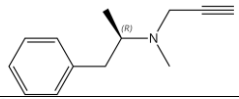
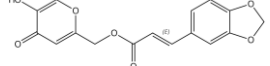
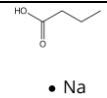
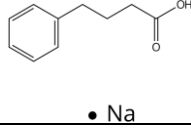
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| Rosmarinic acid | 20283-92-5  | Rosemary                                                                       | Prevents production of ROS and activation of abnormal mPTP provoked by high glucose, cytoC release and caspase-3                                | Antibacterial, antiviral, antioxidant; anti-spasmodic, choleric, hepatoprotective, antitumorigenic                                   |    | 83   | 69  |
| Rutin           | 153-18-4    | Buckwheat, orange, black tea                                                   | HAT inhibitor, p300 inhibitor, PCAF inhibitor, NFkB inhibitor; chelate metal ions such as iron, inhibits Fenton's reaction                      | Strong antioxidant, antiangiogenic                                                                                                   |    | 245  | 183 |
| Salicylic acid  | 69-72-7     | Broccoli, spinach, cauliflower, cucumber, mushroom                             | Decreases production of inflammatory prostaglandins                                                                                             | Anti-aging, anti-inflammatory                                                                                                        |    | 201  | 711 |
| Sirtuin         | 438496-81-2 | Kale, olives, red wine, strawberries                                           | Maintains regular chromatin condensation; repair DNA damage; modulate oxidative stress; repress insulin resistance                              | Anti-aging, calorie mimetic; anti-inflammatory, stress resistance, fat & glucose metabolism, cardiac rhythm, mitochondria biogenesis | N/A                                                                                   | 2235 | 180 |
| Spermidine      | 124-20-9    | Fresh green pepper, wheat germ, cauliflower, broccoli, mushrooms, cheeses      | Autophagy inducing; reduces histone acetylation, lipid metabolism and regulates cell growth and signaling pathways                              | Antioxidant, anti-inflammatory                                                                                                       |    | 235  | 52  |
| Sulforaphane    | 4478-93-7   | Cruciferous vegetables: kale, bok choy, cabbage                                | Detoxifies carcinogens and pro-oxidants by blocking phase I metabolic enzymes; arrests cell cycle to impede cell proliferation; BACE1 inhibitor | Antioxidant, anti-inflammatory, protect DNA                                                                                          |   | 73   | 27  |
| Tretinoin       | 302-79-4    | Natural retinol                                                                | Stimulates mitotic activity, enhances loosely adherent corneocyte turnover                                                                      | Anti-aging agent                                                                                                                     |  | 229  | 319 |
| Ursolic acid    | 77-52-1     | Apple peel, cranberry juice, grape skin, basil, rosemary, thyme, oregano, sage | Insulin secretagogue and insulinomimetic; regulates glucose uptake                                                                              | Antihyperglycemic; insulin sensitivity increase; antioxidant, anti-inflammatory, antibacterial, antifungal                           |  | 69   | 91  |

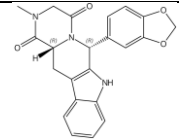
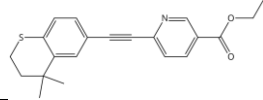
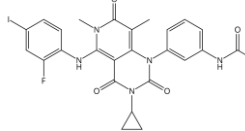
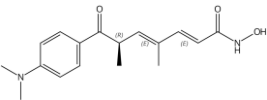
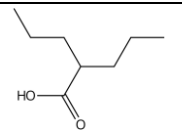
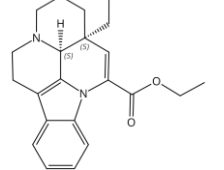
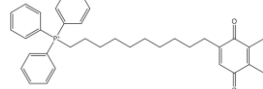
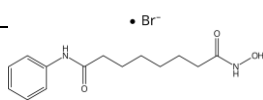
|                             |           |                                                                        |                                                                                                                       |                                                                                                                                          |                                                                                     |      |      |
|-----------------------------|-----------|------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|------|------|
| Vitamin A (Retinol)         | 68-26-8   | Egg yolk, beef liver, carrots, pumpkin, sweet potatoes, mangos, papaya | Important to vision, growth, cell division, reproduction and immunity                                                 | Antioxidant                                                                                                                              |  | 1141 | 934  |
| Vitamin C (L-ascorbic acid) | 50-81-7   | Citrus, blackcurrant, rose hip, guava, chili pepper, parsley           | Enhances collagen synthesis, slow down aging                                                                          | Vital for immune system, heart, blood vessels; antioxidant, anti-hypertensive, immune stimulant; reduces heart disease and dementia risk |  | 2030 | 2482 |
| Vitamin E                   | 1406-18-4 | Nuts, seeds, vegetable oils: corn and soybean                          | Prevents peroxidation of unsaturated fatty acids; important to vision, reproduction, and blood, brain and skin health | Antioxidant                                                                                                                              | N/A                                                                                 | 1593 | 1879 |

**Table S3.** Synthetic anti-aging agents most widely represented in the CAS Content Collection including structures <sup>1-18</sup>

| Synthetic compounds                            | CAS Reg #    | Mechanism of action / Anti-aging strategy                                                                                                                         | Application / Benefits                                                                                 | Structure                                                                             | Number of journal articles | Number of patents |
|------------------------------------------------|--------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------|----------------------------|-------------------|
| 4-hydroxy phenyl N-tert-butyl nitron, CPI-1429 | 223649-80-7  | Blocks signal transduction associated with neuroinflammation enhanced in neurodegenerative disorders                                                              | anti-aging, neuroprotectant                                                                            |    | 2                          | 2                 |
| Acarbose                                       | 56180-94-0   | Synthesized by soil bacteria Actinoplanes sp through its precursor valienamine                                                                                    | Inhibits alpha glucosidase; anti-diabetic for type 2 diabetes                                          |    | 87                         | 19                |
| N-Acetylcysteine                               | 7218-04-4    | Increases cell protection to oxidative stress                                                                                                                     | Flu, dry eye, cough, and other lung conditions                                                         |    | 48                         | 9                 |
| Adapalene                                      | 106685-40-9  | Targets abnormal desquamation of skin and anti-inflammatory properties                                                                                            | Treatment of acne vulgaris                                                                             |    | 7                          | 52                |
| Aspirin                                        | 50-78-2      | Inhibits the activity of cyclooxygenase (COX) which leads to formation of prostaglandins causing inflammation; regulating AMPK and insulin-like signaling pathway | Protects telomeres upon cell reproduction, restrains their shortening and related cell aging and death |    | 3569                       | 162               |
| Azacitidine                                    | 320-67-2     | DNA methyltransferase inhibition by covalent bonding, resulting in DNA hypomethylation                                                                            | Helps bone marrow grow normal blood cells; anti-atherogenic                                            |   | 47                         | 21                |
| AZD8055                                        | 1009298-09-2 | Blocks mTORC1 and mTORC2 signaling in AML                                                                                                                         | Antitumor effect used against neuroblastoma cells                                                      |  | 3                          | 4                 |
| Danazol                                        | 17230-88-5   | Androgen receptor agonist; ovarian steroidogenesis inhibitor; lowers gonadotropin levels in postmenopausal women                                                  | Treats endometriosis and fibrocystic breast disease by shrinking displaced tissue of uterus            |  | 15                         | 5                 |
| Dapagliflozin (Dapagliflozon, Farxiga)         | 461432-26-8  | Inhibits SGLT2 thereby controlling hyperglycemic activity                                                                                                         | Treatment of type 2 diabetes                                                                           |  | 45                         | 9                 |

|                                           |             |                                                                                                                                                 |                                                                                                                                                 |                                                                                       |     |     |
|-------------------------------------------|-------------|-------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------|-----|-----|
| Dasatinib                                 | 302962-49-8 | Inhibits proliferation, adhesion, migration and invasion of HCC cells by inhibiting Src tyrosine kinase and modifying SFK/FAK and PI3K/PTEN/Akt | Treatment of chronic myeloid leukemia                                                                                                           |    | 39  | 21  |
| Elamipretide                              | 736992-21-5 | Targets mitochondrial inner membrane by its enrichment in cardiolipin                                                                           | Anti-aging                                                                                                                                      |    | 4   | 7   |
| Entinostat (SNDX-275; MS-275)             | 209783-80-2 | Class I and IV HDAC inhibitor (HDAC1, 2, 3)                                                                                                     | Antitumor agent; histone deacetylase inhibitor; memory promoter                                                                                 |    | 3   | 11  |
| Epitalon                                  | 307297-39-8 | Pineal gland, retina, brain function regulator, induces neuronal cell differentiation in stem cells                                             | Anti-aging                                                                                                                                      |    | 31  | 1   |
| Ergoloid mesylate (Hydergine)             | 8067-24-1   | Stimulates dopaminergic and serotonergic receptors and blocks alpha-adrenoreceptors                                                             | Treats dementia and age-related cognitive impairment; recovery after stroke                                                                     | N/A                                                                                   | 6   | 2   |
| Human growth hormone (hGH)                | 12629-01-5  | Regulates fat, muscle, tissue, and bone; stimulates the synthesis of chondroitin sulfate and collagen; promotes somatic growth                  | Maintains, builds, and repairs healthy tissue in brain and other organs; speeds up healing after injury and repair muscle tissue after exercise | N/A                                                                                   | 200 | 18  |
| Idebenone                                 | 58186-27-9  | Blocks free radicals damage and sustains normal ATP levels                                                                                      | Alzheimer's disease, cognitive defects                                                                                                          |   | 15  | 49  |
| Isotretinoin                              | 4759-48-2   | Inhibits sebaceous gland function and keratinization                                                                                            | Acne, cutaneous conditions                                                                                                                      |  | 60  | 61  |
| Meclofenoxate (Centrophenoxine, Lucidril) | 51-68-3     | Diminution of lipofuscin content of nerve cell; enhances activity of succinic and lactic dehydrogenase                                          | Memory-boosting                                                                                                                                 |  | 34  | 9   |
| Metformin                                 | 657-24-9    | Inhibits mTORC1 activity; growth hormone suppression                                                                                            | Type 2 diabetes, PCOS; dietary restriction, anti-atherogenic                                                                                    |  | 936 | 105 |

|                                          |             |                                                                                                                      |                                                                                                 |                                                                                       |     |    |
|------------------------------------------|-------------|----------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------|-----|----|
| Panobinostat                             | 404950-80-7 | Inhibitor of class I HDAC; class IIa and IIb HDAC, class IV HDAC; histone deacetylase inhibitor                      | Antitumor agent                                                                                 |    | 5   | 9  |
| Piracetam                                | 7491-74-9   | Improves the function of neurotransmitter acetylcholine via muscarinic cholinergic receptors                         | Neuroprotective, anticonvulsant, improves neural plasticity in cognitive disorders and dementia |    | 43  | 10 |
| Procaine (Gerovital H3, GH3, KH-3)       | 59-46-1     | Inhibits Na influx across voltage gated Na-channels in neuronal cell membrane of peripheral nerves                   | Anti-inflammatory, analgesic, vasodilatation, antioxidant; nervous system balance               |    | 60  | 35 |
| Pyridopyrimidines                        | -           | High affinity DHFR inhibitor, thus decreasing tetrahydrofolate quantity required for pyrimidine and purine synthesis | KRAS inhibitors; anticancer                                                                     | N/A                                                                                   | 1   | 0  |
| Rosiglitazone                            | 122320-73-4 | Inhibits PPAR-γ activity                                                                                             | Indicated for treatment of type 2 diabetes                                                      |    | 57  | 30 |
| Ruxolitinib                              | 941678-49-5 | Inhibits JAK1 and JAK2, block dysregulated cell signaling, prevent abnormal blood cell proliferation                 | Treatment of myelofibrosis in adults                                                            |    | 23  | 8  |
| Salsalate                                | 552-94-3    | Decreases formation of prostaglandins involved in pain, fever, inflammation                                          | Anti-inflammatory, antirheumatic                                                                |    | 4   | 13 |
| Selegiline (L-deprenyl, Eldepryl, Emsam) | 14611-51-9  | Selective inhibitor of MAO-B                                                                                         | Treats symptoms of Parkinson's disease and major depressive disorder                            |   | 109 | 28 |
| Seletinoid G                             | 637357-50-7 | Type I procollagen, tropoelastin, and fibrillin-1 expressions stimulation, reduces MMP-1                             | Anti-aging                                                                                      |  | 4   | 2  |
| Sodium butyrate                          | 156-54-7    | Suppresses NFκB activation, inhibits interferon γ production and upregulation of PPARγ                               | Antioxidant, anti-inflammatory, autophagy inducing                                              |  | 37  | 17 |
| Sodium phenylbutyrate (Buphenyl)         | 1716-12-7   | Inhibitor of class I HDAC, class IIa HDAC and class IIb HDAC                                                         | Antitumor agent; memory enhancement; amyloid burden reduction                                   |  | 7   | 8  |

|                |             |                                                                                                                                                        |                                                                                                                                         |                                                                                       |     |    |
|----------------|-------------|--------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------|-----|----|
| Tadalafil      | 171596-29-5 | PDE 5 inhibitor with potent anti-aging activity                                                                                                        | Treats erectile dysfunction and benign prostatic hyperplasia                                                                            |    | 7   | 11 |
| Tazarotene     | 118292-40-3 | Binds to retinoic receptor and modify gene expression                                                                                                  | Used for psoriasis, acne, and psoriatic arthritis                                                                                       |    | 7   | 34 |
| Trametinib     | 871700-17-3 | ERK phosphorylation inhibitor, Ki67 suppression, tumor growth inhibition with mutant BRAF or RAS decreasing, G1 cell cycle arrest, apoptosis induction | Applied alone or in combination with dabrafenib to treat skin cancer (melanoma), thyroid cancer, and non-small cell lung cancer (NSCLC) |    | 7   | 4  |
| Trichostatin A | 58880-19-6  | Inhibitor of class I HDAC, class IIa HDAC, class IIb HDAC6                                                                                             | Antifungal, antibacterial, histone deacetylase inhibitor; protein synthesis inhibitor; antitumor, memory enhancement                    |    | 28  | 4  |
| Valproic acid  | 99-66-1     | Inhibitor of class I HDAC                                                                                                                              | Anticonvulsant, mood stabilizer; histone deacetylase inhibitor; GABA modulator; memory enhancement; CDK5 inactivation                   |    | 148 | 23 |
| Vinpocetine    | 42971-09-5  | Selective inhibitor of Ca(2+)-calmodulin dependent cGMP-PDE                                                                                            | Memory enhancer; against dementia, stroke, hearing loss                                                                                 |   | 10  | 8  |
| Visomitin      | 934826-68-3 | Penetrates cellular membrane, accumulates in mitochondrial membrane inner leaflet where it is reduced or recharged                                     | Treats inflammation associated with ophthalmic disease: dry eye, corneal wounds                                                         |  | 13  | 3  |
| Vorinostat     | 149647-78-9 | Inhibitor of class I HDAC, class IIb HDAC                                                                                                              | Antitumor, memory enhancement                                                                                                           |  | 22  | 21 |

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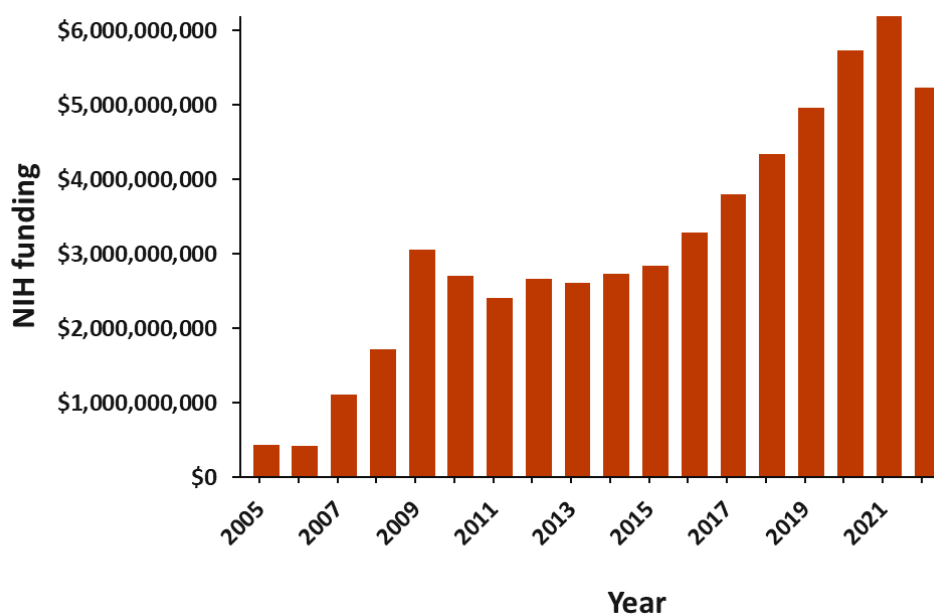
## Anti-aging Strategies and Remedies: A Landscape of Research Progress and Promise

Rumiana Tenchov, Janet M. Sasso, Xinmei Wang, Qiongqiong Angela Zhou\*

CAS, a division of the American Chemical Society

2540 Olentangy River Rd, Columbus, OH 43202, USA

**Figure S1.** Yearly NIH funding for projects related to anti-aging research.



**Figure S1.** Yearly NIH funding for projects related to anti-aging research.