A Nanorobotic Approach for Aiding Alzheimer's Disease

M. Anju Rajan*

G. Pulla Reddy College of Pharmacy; Hyderabad, India

Abstract: *Nanorobotics is a field which is changing vision of pharmaceutical and medical sciences. The conventional drug delivery systems do not provide cyto-architectural restoration and connection patterns that are crucial for functional recovery in neurodegenerative disorders due to limitations posed by the restrictive Blood-Brain Barrier (BBB). Nerveborne nanorobots carry and deliver drugs to affected neuronal cells crossing the BBB. Manipulation of nanorobots is extensively carried out to treat Alzheimer's Disease where there is destruction of neuronal cells. They are used to restore the functions of oligodendrocytes due to demyelination of neurons in white mater. The aim of this article is to present the future use of nanorobots to combat Alzheimer's Disease.*

Keywords: Nanorobots, Blood-Brain Barrier, Oligodendrocytes, Alzheimer's Disease

1. Introduction

Alzheimer disease (AD) is a progressive neurodegenerative disease, which causes the degeneration, or loss of neurons in the brain, particularly in the cortex. This leads to symptoms characteristic of dementia. Although the cause of Alzheimer's isn't completely understood, two major players that are often cited in its progression are plaques and tangles. Due to restrictive Blood-Brain Barrier, conventional drug delivery systems cannot deliver the required therapeutic effect. As a result, nanorobotic technology was developed to carry and deliver drugs to the specific infected neuronal cells bypassing the blood-brain barrier.

Nanorobots
Nanorobots are tiny sophisticated machines designed to perform specific task repeatedly with precision at nanoscale dimensions. The exterior of the nanorobot is composed of a diamondoid material to which may be connected to an artificial glycocalyx surface that minimizes fibrinogen (and other blood proteins) adsorption and bioactivity, ensuring sufficient biocompatibility to avoid immune system attack.

Structure:
A nanorobot consists of the following parts:
Microprocessor- it controls the overall operations of the nanorobot.
Magnetic switch- is used to provide switch ON and OFF of the nanorobot at any point of time.
Manipulators- provides the torque to move and control the speed of the nanobot.
Payload- it is the void section that holds the required dose of drug, which is delivered at the site of action.
Power source- it consists of nano circuits that provide electromagnetic energy, to ensure energy as long as necessary to keep the nanorobot in operation.
Motor- is responsible for propagation of the nanorobot inside the circulatory system in the blood vessels.
Sensors- internal sensors detect specific chemicals released by the affected cells, thereby directing the nanorobot to the target site.
Micro Camera- a miniature camera helps the operator to steer the nanorobot for navigating through the body manually.

Size
Nanorobots are devices typically ranging in size from 0.1-10 micrometres and constructed of nanoscale or molecular components, in order to enable their easy penetration into capillaries, cells, neurons.

Features
1) Specific site of action.
2) Require minimum operational energy.
3) Posses greater durability
4) Operate at high speeds.

2. Pathophysiology of Alzheimer's Disease

2.1 Amyloid Plaque Pathology

In the cell membrane of a neuron in the brain, a molecule called Amyloid Precursor Protein or APP is present. One end of APP lies within the cell and the other end lies outside the cell. APP is critical for neuronal growth, survival and post-injury repair. Since APP is a protein, just like other proteins, it gets used and over time it gets broken down and recycled. Generally, it is cleaved by an enzyme called Alpha Secretase and Gamma Secretase. The cleaved peptide is soluble and gets degenerated. But, if APP cleaved is by the enzyme Beta secretase along with Gamma secretase, the fragment resulted is not soluble and creates a monomer called Amyloid Beta. These monomers tend to be chemically "sticky", and bond together outside the neurons as clumps called Beta-Amyloid Plaques. These plaques can potentially get between the neurons, which can get in the way of neuron-to-neuron signaling. If the brain cells are unable to signal and relay information, then the brain functions like memory can be seriously impaired. The plaques generated can start up an immune response and cause inflammation which might damage surrounding neurons. Amyoid plaque can also deposit around blood vessels in the brain, called amyloid angiopathy, which weakens the walls of blood vessels and increases the risk of hemorrhage, or rupture and blood loss.

2.2 Tau Protein Pathology

Every neuron has a cytoskeleton, an internal support structure partly made up of structures called microtubules. These microtubules act like tracks, guiding nutrients and molecules from the body of the cell to the axonal ends and back. Tau protein is a microtubule-associated protein, expressed in neurons and glia, that stabilizes microtubules in the cell cytoskeleton – especially in axons, where it appears to play a role in establishing neuronal polarity and axonal identity. Although again, not completely understood, it's thought that the beta amyloid plaque build-up outside the neuron initiates pathways within the neuron that leads to activation of Kinase, an enzyme that transfers phosphate groups to the tau protein. The hyperphosphorylated tau protein then changes shape, stops supporting the microtubules, and clumps up with other tau proteins, or gets tangled, and leads to the formation of Neurofibrillary Tangles which is the other characteristic finding of Alzheimer Disease. Neurons with tangles and non-functioning microtubules cannot signal well, and sometimes end up undergoing Apoptosis, or programmed cell death.

2.3 Lipofuscin Pathology

Yellow-brown insoluble age-pigment of lysosomal digestion called "lipofuscin" may collect in many of our cells. Mitochondrial autophagocytosis is believed to be a major contributor to lipofuscin formation. Lipofuscin is likely the product of the oxidation of unsaturated fatty acids and may be symptomatic of membrane damage or damage to mitochondria and lysosomes. Lipofuscin granules are composed of lipid containing residues of lysosomal digestion, usually arranged around the cell nucleus. The accumulation of such lipochromes starts as early in life as 11 years old and rises with age, activity level, and caloric intake, and varies with cell type. Clumps of these yellow-brown autofluorescent granules, typically 1-3 microns in diameter – may occupy from 20% of brainstem neuron volume at age 20 to as much as 50% of cell volume by age 90. Pathological accumulation of lipofuscin has been implicated in Alzheimer's disease, as the release of lipofuscin into the extracellular space following the death of neurons could substantially contribute to the formation of Amyloid beta senile plaques leading to Alzheimer's disease. All the above mentioned pathophysiologies, ultimately results in death of neurons, leading to large scale changes in brain which majorly accounts to brain atrophies, or shrinks.

3. Four Progressive Stages of Alzheimer's Disease

Stage 1: Pre-dementia: The first symptoms are often mistakenly attributed to aging or stress. The most observable symptom is short term memory loss, which shows up as inability to acquire new information and difficulty in remembering recently learned facts. Subtle problems with the executive functions of attentiveness, abstract thinking, planning and flexibility or impairments in semantic memory (memory of meanings and concept relationships) are symptomatic of the early stages of Alzheimer's. Apathy is observed at this stage, and remains the most persistent neuropsychiatric symptom throughout the course of the disease. The preclinical stage of Alzheimer's has also been termed mild cognitive impairment (MCI), which is often found to be a transitional stage between normal aging and dementia. When memory loss is the predominant symptom, MCI is termed as "Amnestic MCI" and is frequently seen as a prodromal stage of Alzheimer's disease.

Stage 2: Early AD: In this stage, the person with Alzheimer's is usually capable of communicating basic ideas adequately. While performing fine motor tasks, certain movement coordination and planning difficulties (apraxia) may exist, but they are usually unnoticed. Language problems are mainly characterized by a shrinking vocabulary and decreased word fluency, leading to impoverishment of oral and written language. AD does not affect all memory capacities equally. Episodic memory (Older memories of the person's life), Semantic memory (facts learned) and Implicit memory (the memory of the body on how to do things, such as using a fork to eat) are affected to a lesser extent than new facts or memories.

Stage 3-Moderate AD: Progressive deterioration eventually hinders independence, leading to inability to perform most common activities of daily living. Speech difficulties become evident due to an inability to recall vocabulary, often leading to incorrect word substitutions (paraphasia). Reading and writing skills are also progressively lost. Complex motor sequences become less coordinated. During this period, memory problems worsen and the patient may fail to recognize close relatives. Long-term memory, whichwas previously intact, becomes impaired. Behavioral and neuropsychiatric changes become more prevalent. Common manifestations are wandering, irritability and labile affect (i.e., emotions easily aroused or freely expressed), leading to crying, outbursts of unpremeditated aggression, or resistance to caregiving.

Stage 4: Advanced AD: During the final stage, the patient is completely dependent upon caregivers. Language is decreased to simple phrases or even single words, eventually leading to complete loss of speech. Aggressiveness, extreme apathy and exhaustion are much more common symptoms. The patient will eventually be unable to perform even the simplest tasks independently. Muscle mass and mobility deteriorate to the point where patients are bedridden and unable to feed themselves. The immediate cause of death is usually an external factor (e.g., infection from pressure ulcers, pneumonia).

3. Why does Alzheimer's occur in some people and not others?

AD can be split into groups- Sporadic and Familial.
Sporadic is used to describe the late onset type where the exact cause isn't very well defined, and is probably a combination of genetic and environmental risk factors. Sporadic accounts for the vast majority of cases. With sporadic Alzheimer's, the risk increases significantly with age, affecting around 1% of people aged 60-65, and 50% of people over the age 85. In fact, a gene that's been identified as possibly contributing to an increased risk of AD is the e4 allele of apolipoprotein E gene or APOE-e4. Researchers have shown that the risk of developing AD increases for patients that inherit one e4 allele, and increases even more

for patients who inherited two e4 alleles, one from each parent. Apolipoprotein E helps in breakdown of beta-amyloid, but e4 allele seems to be less effective than other alleles, like the APOE-e2 allele, which implies patients with APOE-e4 allele are more likely to develop beta-amyloid plaques.

Familial AD is used to describe cases where some dominant gene was inherited that speed up the progression of the disease, so sometimes familial AD is referred to as early onset Alzheimer's. Familial accounts for between 5 and 10% of the cases, and can be caused by several gene mutations. First, mutations in the PSEN-1 or PSEN-2 genes on chromosome 14 or chromosome 1, respectively, have been linked to early onset Alzheimer's. These genes encode for Presenilin-1 or Presenilin-2, both protein subunits of the enzyme gamma secretase. Mutations in these PSEN-1 or PSEN-2 genes can change the location where gamma secretase cleaves Amyloid Precursor Protein, producing different length Beta-Amyloid molecules, which seem to be better at clumping up and forming plaques. Another known genetic cause of Alzheimer's is trisomy 21, or Down's syndrome, which involves an extra copy of chromosome 21. It turns out that the gene responsible for producing APP is located on chromosome 21, which means that people with Down's Syndrome have an extra APP gene, and so presumably increased expression of APP gene, potentially increases the amount of a plaque buildup. For this reason, Familial Alzheimer Disease often progresses by age 40. Symptoms of Alzheimer disease worsen as plaques and tangles build up, and neuronal damage accumulates. In the early stages, symptoms may not even be detectable, as it progresses, patients lose short term memory. They then progress to loss of motor skills, making things like eating difficult without help. Also language becomes affected, making it more difficult to communicate. Eventually they lose long-term memory and progressively become more disoriented, which can be dangerous. In late-stage, they become bedridden, and the most common cause of death might be an infection like, pneumonia. Diagnosis of AD is really tough, because the only way to definitively show that a person has Alzheimer's is by performing a brain biopsy after autopsy. Usually a clinician will therefore make a diagnosis after excluding other causes of dementia.

Currently, there isn't any cure for AD, some medications exist which are mainly focused on symptomatic relief, but the benefits are small and there haven't been any medications that clearly and definitively halt the progression of Alzheimer's disease.

4. Conventional Treatment for Alzheimer's Disease

Currently, there isn't any known cure for Alzheimer's disease. Available treatments offer relatively small symptomatic benefit and remain essentially palliative in nature. The current pharmaceutical treatment includes five medications which are employed to treat the cognitive problems of Alzheimer's disease. The first four FDA-approved drugs are Acetylcholine esterase inhibitors which include **Donepezil**, **Galantamine**, **Rivastigmine** and

Tacrine. Reduction in activity of cholinergic neurons is a well-known feature of Alzheimer's Disease. Acetylcholinesterase inhibitors act by reducing the rate at which acetylcholine (Ach) in broken down, thereby increasing the concentration of Ach in brain and combating the loss of Ach caused by the death of cholinergic neurons. The fifth approved drug, **Memantine**, is an NMDA receptor antagonist. Glutamate is a useful excitatory neurotransmitter of the nervous system, although excessive amounts in the brain can lead to cell death through a process called excitotoxicity which consists of the overstimulation of glutamate receptors. Excitotoxicity occurs not only in Alzheimer's disease, but also in other neurological diseases such as Parkinson's and multiple sclerosis. Memantine is a noncompetitive NMDA receptor antagonist which acts on the glutamatergic system by blocking NMDA receptors and inhibiting their overstimulation by glutamate. However, the benefit from the use of any of these five approved drugs is small. Reported side effects include include hallucinations, confusion, dizziness, headache and fatigue. Other medications often used as near-palliatives for Alzheimer's disease include Antidepressant drugs (Citalopram, Fluoxetine), Anxiolytic drugs (Lorazepam, Alprazolam). So far, no medication has been clearly shown to significantly delay or halt the progression of the disease.

5. New Approach: Medical Nanorobotics

1. Chromallocyte
"Chromallocyte" is a hypothetical mobile cell-repair nanorobot with the primary purpose of performing Chromosome Replacement Therapy (CRT). In CRT, the entire chromatin content of the nucleus in a living cell is extracted and promptly replaced with a new set of prefabricated chromosomes that have been artificially manufactured as defect-free copies of the originals. Replacement chromosome sets would be manufactured in a desktop *ex vivo* chromosome sequencing and manufacturing facility, then loaded into the nanorobots for delivery to specific targeted cells during CRT. The chromallocyte will be capable of limited vascular surface travel into the capillary bed of the targeted tissue or organ, followed by diapedesis (exiting a blood vessel into the tissues), histonatation (locomotion through tissues), cytopenetration (entry into the cell interior), and complete chromatin replacement in the nucleus of the target cell. The CRT mission ends with a return to the vasculature and subsequent extraction of the nanodevices from the body at the original infusion.

2. Microbivore:
"Microbivore" is an artificial nanorobotic white cell substitute that can seek out and harmlessly digest the beta-amyloid plaques, tau tangles and lipofuscin granules. They can perform phagocytosis and microbial killing equivalent to WBC at much faster operational and reliable rate, under human control. It can safely pass through even the narrowest of human capillaries and elsewhere in the human body. A microbivore has an ingestion port, where the intracellular and extracellular aggregates are fed in to be digested and an exhaust port, where the completely digested remains of the aggregates are harmlessly expelled from the device. Plaque

binding sites and binding sites for phosphorylated tau protein can be installed on the external recognition modules of tissue-mobile microbivore-class scavenging nanorobots, allowing them to quickly seek, bind, ingest, and fully digest existing beta-amyloid plaques and tau tangles throughout the relevant tissues, in the manner of artificial mechanical macrophages. When treatment is finished, the doctor may transmit an ultrasound signal which leads the nanorobots to exit the body through the kidneys and be excreted with the urine in due course.

Medical Nanorobots: Ingress to, and Egress from, the Brain

A decisive capability for medical nanorobots intended for neural repair is the ability to harmlessly enter and exit the live brain tissue of the patient. Entry to brain tissue by large molecules and particulate matter is restricted by the presence of three distinct interfaces through which medical nanorobots seeking access must pass. These interfaces are called, respectively, the blood-brain barrier or BBB that separates the blood from direct contact with brain tissue, the blood-cerebrospinal fluid barrier or BCB that separates the blood from direct contact with cerebrospinal fluid in the brain ventricles and spinal column, and finally the CSF-brain interface or ependymal interface that separates the CSF from the brain tissue or neuropil.

Blood-Brain Barrier (BBB) Penetration:

The blood-brain barrier (BBB) is a highly selective permeability barrier, formed by tight junction brain endothelial cells, that separates the circulating blood from the neuropil of the brain in which the neurons reside. The BBB largely prevent diffusion of microscopic objects (bacteria) and large hydrophilic molecules into CSF while allowing diffusion of small hydrophobic molecules and active transport of metabolic chemicals such as glucose through the endothelial membrane into the brain. To accomplish cure for Alzheimer's disease, medical nanorobots should penetrate through the BBB which is achieved through the following methods:

1) **Localised Osmotic Disruption** via intracarotid infusion of hypertonic saccharide solution, (e.g., mannitol, arabinose or alkyl-glycerol), resulting in transient shrinkage of cerebrovascular endothelial cells with widening of the tight junctions, thereby increasing permeability of the BBB.
2) **Acoustic and Thermal Disruption.** High intensity focused ultrasound near the target endothelium, creates mechanical stress on the endothelial tight junctions, causing them to open and admit therapeutic agents into the brain.
3) **Exploit unbarriered pathways:** A amall number of regions in the brain do not have BBB, or have a vascular endothelium that lacks tight junctions (i.e., the maxillary branch of the trigeminal nerve) that initiate in the brain and terminate in the nasal cavity at the olfactory neuroepithelium. These are the only externally exposed portions of the central nervous system and therefore represent the most direct method of noninvasive entry of the nanorobots into the brain by bypassing BBB.
4) **Diapedesis with Cytocarriage:** The commandeering of natural motile cells by medical nanorobots, known as cytocarriage, offers another alternative mode of *in vivo*

transport. During cytocarriage, one or more medical nanorobots may enter a motile cell (mesenchymal stem cells and leukocytes including monocytes and neutrophils), ride or steer the cell to a desired destination inside the human body, then vacate the cell upon arrival, without destroying the tight junction integrity of the BBB.
5) **Direct Cytopenetration:** Even in complete absence of all the aforementioned methods, properly mission-designed active nanorobots can employ a combination of cytopenetration, *in cyto* locomotion and histonatation through the vascular endothelium of the BBB to achieve ready access to the neuropil.
6) **Direct Injection into the Brain:** As a last resort, a sharp needle or microcatheter can be passed directly through the skull or entirely through soft tissues (to avoid skull penetration), terminating precisely inside the neuropil or specialized tissue masses and allowing medical nanorobots to ingress or egress via that route.

Blood-CSF Barrier (BCB) Penetration

Cerebrospinal fluid (CSF) is a clear, colorless fluid occurring in the brain and spinal cord. The CSF system offers an alternate route into the brain for blood borne medical nanorobots. To enter the CSF system from the bloodstream, the nanorobots must pass through the blood-CSF barrier (BCB) – a pair of barriers that separates peripheral and cerebral blood flow from the cerebrospinal fluid. Penetration through the BCB is achieved by the following methods:

1) **BBB Penetration Methods.** Any of the methods previously identified for possible use by medical nanorobots to penetrate the blood-brain barrier could also be applied to the tight-junction barrier that exists between the choroid plexus epithelial cells comprising the BCB.
2) **Lumbar Injection.** Lumbar puncture is carried out under local anesthesia sterile conditions by inserting a needle into the subarachnoid space, usually between the third and fourth lumbar vertebrae. Medical nanorobots could be inserted into, or extracted from the needle.
3) **Intraventricular Injection:** Medical nanorobots can be inserted into the CSF, by an intrathecal injection along with a direct injection into the four cerebral ventricles by a ventricular catheter system.

6. Nanorobotic treatment-The Alzheimer Protocols

The proposed nanorobotic treatment for Alzheimer's disease can be conceptually organized as a series of three specific protocols which are aimed at three distinct clinical objectives. These objectives are: Genetic Derisking, Tissue Rejuvenation and Neural Reconstruction.

First Alzheimer protocol: Genetic Derisking.

Each patient is fully genotyped using gene sequencing technology. Upon full genotyping and analysis, it may be discovered that the patient has inherited a small subset of genes that increase the person's risk of developing Alzheimer's Disease, possibly at an early age. Some of the patients might already be displaying clinical signs of Alzheimer's. All such genetically at-risk patients should first be treated with a gene editing procedure (CRISPR

techniques), to correct these inherited genetic defects that produce increased susceptibility to Alzheimer's. Required genetic corrections may include replacement of familial Alzheimer's disease gene mutations, replacement of apolipoprotein ApoE4 genes and other high risk genes, and elimination of Alzheimer's related pathological genetic mosaicism. Once identified, all required genetic corrections can be applied in a single procedure directed to all relevant target cells.

For the genetic derisking protocol, the patient's genotype will be analyzed and edited, resulting in a corrected (derisked) genotype sequence. Working from this corrected data file, replacement chromosome sets will be fabricated in an *ex vivo* desktop chromosome manufacturing facility, then loaded into billions of chromallocyte nanorobots for delivery to every one of the patient's affected cells. These replacement sets will contain chromosomes from which the defective genes that lead to AD have been deleted and replaced with nondefective genes. For instance, correcting high-risk genes that are present in all of the patient's neurons would require an injected dose of 86 billion chromallocyte nanorobots that can individually target each of the 86 billion neurons in the human brain, with each nanorobot delivering one complete replacement chromosome set into the nucleus of every neuron.

Second Alzheimer Protocol: Tissue Rejuvenation
The natural progress of aging gradually reduces the effectiveness of the biochemical pathways that control the normal processing and degradation of proteins, leading to a failure of proteostasis and subsequently to the accumulation of excess Amyloid beta plaques, tau protein, and a cascade of pathological biochemical events, manifesting eventually in the clinical symptoms of Alzheimer's disease. The use of medical nanorobots to arrest accumulative age-related damage is described in two major categories as: removing extracellular aggregates, removing intracellular aggregates.

Removal of Extracellular Aggregates:
Extracellular aggregates (Beta-Amyloid plaques) are biochemical byproducts, with no further useful physiological or structural function, that have been aggregated into deposits outside the cell. The most notorious insoluble extracellular aggregates in the Alzherimer's patient brain are the toxic amyloid plaques. Specific regions of brain like the amygdala, the hippocampus, and certain regions of the cortex appear more prone than others to produce plaques. The pathophysiology of Beta Amyloid Plaque formation is mentioned above.

Plaque binding sites can be installed on the external recognition modules of tissue-mobile microbivore-class scavenging nanorobots, allowing them to quickly seek, bind, ingest, and fully digest existing amyloid plaques throughout the affected tissues, in the manner of artificial mechanical macrophages. The nanorobot can incorporate mechanisms and mechanical procedures designed to avoid damage to key extracellular structures while the plaque is being extracted and digested.

Removal of Intracellular Aggregates:
Intracellular aggregates are highly heterogeneous lipid and protein biomaterials that have accumulated and aggregated into clumps inside of the cell. Intracellular aggregates often accumulate inside lysosomes, organelles that contain the most powerful degradation machinery in the cell. But if the lysosomes become congested and engorged, the cell will stop working properly. Nanorobotic clearance of intracellular aggregates, the greatest concern in Alzheimer affected brain include: (1.) Neurofibrillary Tangles (NFTs) or "tau tangles" composed mostly of hyperphosphorylated tau protein, (2.) Lipofuscin Granules.

Binding sites for Intracellular aggregates (phosphorylated tau protein or Neurofibrillary tangles or Lipofuscin granules) can be installed on the external recognition modules of tissue-mobile microbivore-class scavenging nanorobots, allowing them to quickly seek, bind, ingest, and fully digest the intracellular aggregates throughout the relevant tissues, in the manner of artificial mechanical macrophages.

Third Alzheimer Protocol: Neural Reconstruction
With genetic susceptibilities eliminated, accumulated damage repaired, and existing cells and tissues rejuvenated into a relatively youthful state on a recurring schedule, the process of reconstructing any neural tissue that is either too damaged to repair or has been destroyed is initiated. For effective cell replacement strategies for Alzheimer's, neural stem cells would first need to migrate to multiple areas of the brain and then differentiate and mature into multiple neuronal subtypes. These neurons would then need to re-innervate appropriate targets and establish physiologically relevant afferent connectivity, in essence recapitulating much of the complex brain circuits. It will be difficult, if not impossible, to meet all of the requirements using treatments with stem cells alone. However, we can meet all of the requirements using nanorobots.

Third Alzheimer Protocol begins with extensive brain mapping and the compilation of a neural repair plan. The next step is reconstruction of the missing neural tissue. Reconstruction requires manufacturing replacement neural cells, debridement of neural detritus in heavily damaged or envoided areas, insertion and emplacement of replacement cells via a nanocatheter array, and incorporation of the replacement cells into the existing neural tissues. Finally, full incorporation is elicited and guided by an intensive program of neural network retraining, enabling significant restoration of function to the Alzheimer's patient. Network retraining relies on the experimentally-proven beneficial effects of environmental enrichment, which includes activities designed to elicit recovery of brain memory data and mental algorithms.

Other Applications of Nanorobots
1) Respirocyte nanorobots have the ability to deliver 236 times more oxygen to the tissues per unit volume than natural red cells. Hence, it could use in treatment of various lung and perinatal/neonatal disorders.
2) In treating artherosclerosis, where nanorobots are used to chip away plaques along the arterial wall. They cut away the plaques by releasing antithrombotic drug like clopidogrel.

3) Breaking up blood clots.
4) In fighting cancer. They attack the tumour cells directly using lasers, microwaves and ultrasonic signals or aid in chemotherapy by acting as a carrier for chemotherapeutic drugs, thereby achieving active cell targeting.
5) To augment our immune system. Nanorobots (Microbivore) can wage a micro-war against parasitic organisms and on pathogens.
6) To treat Gout. The nanorobot chips out the uric acid crystals accumulated at joints, though it wouldn't be able to reverse the condition permanently.
7) To break kidney stones. Nanorobots carry small ultrasonic signal generators to deliver frequencies directly to kidney stones.

7. Conclusion

Alzheimer's disease (AD), along with many other neurodegenerative disorders, is presently incurable despite many decades of research and many billions of dollars invested in the effort. Future developments of conventional technologies now on the long-term R&D horizon – including pharmaceuticals, nanoparticles, gene therapies, stem cells, and anti-aging drugs will require huge investments, many decades of further development, and seem to highly fail in providing a complete cure. These devices will make it possible to treat and cure previously untreatable and incurable diseases. Medical nanorobots will provide a single powerful general-purpose therapeutic platform that can at the same time address many different kinds of biological malfunctions, using platform variants specifically and efficiently targeted to each of the multifactorial pathologies comprising Alzheimer's disease.

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