**Supplementary Table1: Description of the Classes and Sub-classes from the MeSH hierarchy which were considered for creation of the refined MeSH terms**

|  |  |  |
| --- | --- | --- |
| **Class** | **Selected subclasses** | **Rationale** |
| A | A11 | Terms referring to anatomy can be closely related/tagged with few drugs, as they may help identify target locations of ailment/therapy. Other drugs which are used for treatments in similar system/location (e.g.- gastrointestinal, cardiac etc.) can thus be identified. Anatomical keywords may also help identify drugs which act in different parts of body, but may have similar targets, such as the term 'Endothelium/Endothelial' [26] can be closely related with drugs treating hypertension, as well as with drugs treating other ailments such as stroke, sepsis, Adult Respiratory distress Syndrome etc.    Names of cells/cellular structures can be ambiguous and overlapping in different cases. However anatomical terms specifically related to each system such as Digestive, Nervous etc. may not be as useful. The recurrence of Cellular Anatomical keywords in MeSHDD generated keywords is another reason to select A11 |
| C | All | Names of diseases and their symptoms carry valuable information from repurposing perspective. For example, a drug may treat certain symptom of one disease which might be part of progression of an entirely unrelated disease. For example - Lung Abscess, Kidney Abscess and Skin Abscess. |
| D | All | Drugs belonging to same class of chemicals such as Pyrroles, Aza etc. may have similarities in mechanism of action and drug target profile [27]. Such candidates can be further investigated for repurposing for each other's targeted diseases.    Another way in which list of Chemicals can be used for repurposing, is for identifying similar biological chemicals involved in disease progression or therapy such as Platelet Activated Factor [28], Histamine etc. |
| E | E01 and E02 | Certain terms related to diagnostic tests which may be used in diverse diseases can be used for establishing link between drugs, for example - Lymphocyte count, CD4-CD8 ratio, cell migration assay [29], transplantation etc.    Terms related to Diagnosis of conditions can be used for connecting different conditions. Such terms have recurred in MeSHDD generated keywords also    Details of Therapeutic approaches may also be useful for linking diseases of dissimilar origins, such as transplantation etc. |
| G | G02-05, G07-12 | Processes belonging to Chemical (Amination, Protein folding etc.) or Biochemical (Gluconeogenesis, Lipolysis etc.) [30] categories can be used for linking drugs on basis of mechanism of action. However, categories such as Physical and Plant physiological phenomena can be completely ignored.    The sub-classes selected here can be divided into two categories, Cellular phenomena and Bodily phenomena. Cellular phenomena can be used for linking different diseases and drugs using specific mechanisms of action/disease progression etc. Bodily physiological phenomena can be used for linking drugs and diseases having similar phenotypic manifestations. |

**Supplementary Table 2. Description of drugs which have been previously suggested for repurposing and could also be predicted using results of various in silico experiments conducted using k-means clustering**

|  |  |  |  |
| --- | --- | --- | --- |
| **K-means Clustering** | In silico Experiment 1 | In silico Experiment 2 | In silico Experiment 3 |
| **Drug name** | **Raloxifene hydrochloride** | **Raloxifene hydrochloride** | **Raloxifene hydrochloride** |
| Cluster# | 17 | 17 | 17 |
| Original Indication | Osteoporosis | Osteoporosis | Osteoporosis |
| Original indication drug | Testosterone, Nandrolone | Testosterone, Nandrolone | Testosterone, Nandrolone |
| Repurposed Indication | Cancer | Cancer | Cancer |
| Repurposed Indication Drug | Megestrol | Megestrol | Megestrol |
| **Drug name** |  | **Dapsone** | **Dapsone** |
| Cluster# | 7 | 5 |
| Original Indication | Leprosy | Leprosy |
| Original indication drug | Prednisone | Prednisone |
| Repurposed Indication | Malaria | Malaria |
| Repurposed Indication Drug | Hydroxychloroquine | Hydroxychloroquine |

**Supplementary Table 3.**  **Description of drugs which have been previously suggested for repurposing and could also be predicted using results of various in silico experiments conducted using hierarchical clustering**

|  |  |  |  |
| --- | --- | --- | --- |
| **Hierarchical Clustering** | In silico Experiment 1 | In silico Experiment 2 | In silico Experiment 3 |
| **Drug name** | **Raloxifene hydrochloride** | **Raloxifene hydrochloride** | **Raloxifene hydrochloride** |
| Cluster# | **11** | **17** | **9** |
| Original Indication | Osteoporosis | Osteoporosis | Osteoporosis |
| Original indication drug | Testosterone, Nandrolone | Testosterone, Nandrolone | Testosterone, Nandrolone |
| Repurposed Indication | Cancer | Cancer | Cancer |
| Repurposed Indication Drug | Megestrol | Megestrol | Megestrol |
| **Drug name** | **Dapsone** | **Dapsone** | **Dapsone** |
| Cluster# | 24 | 25 | 22 |
| Original Indication | Leprosy | Leprosy | Leprosy |
| Original indication drug | Rifampin (also known as Rifampicin) | Rifampin (also known as Rifampicin) | Rifampin (also known as Rifampicin) |
| Repurposed Indication | Malaria | Malaria | Malaria |
| Repurposed Indication Drug | Sulfadiazine | Sulfadiazine | Sulfadiazine |
| **Drug name** | **Metformin** | **Metformin** | **Metformin** |
| Cluster# | 36 | 14 | 14 |
| Original Indication | Diabetes | Diabetes | Diabetes |
| Original indication drug | Glimepiride | Glimepiride | Glimepiride |
| Repurposed Indication | Cancer | Cancer | Cancer |
| Repurposed Indication Drug | Streptozocin | Streptozocin | Streptozocin |
| **Drug name** | **Pioglitazone** | **Pioglitazone** | **Pioglitazone** |
| Cluster# | 36 | 14 | 14 |
| Original Indication | Diabetes | Diabetes | Diabetes |
| Original indication drug | Glimepiride | Glimepiride | Glimepiride |
| Repurposed Indication | Cancer | Cancer | Cancer |
| Repurposed Indication Drug | Streptozocin | Streptozocin | Streptozocin |
| **Drug name** | **Tamoxifen** | **Tamoxifen** | **Tamoxifen** |
| Cluster# | 20 | 20 | 18 |
| Original Indication | Cancer | Cancer | Cancer |
| Original indication drug | Ramucirumab | Ramucirumab | Ramucirumab |
| Repurposed Indication | Antimicrobial | Antimicrobial | Antimicrobial |
| Repurposed Indication Drug | Rifabutin | Rifabutin | Rifabutin |
| **Drug name** | **Eflornithine** | **Eflornithine** |  |
| Cluster# | 20 | 20 |  |
| Original Indication | Cancer | Cancer |  |
| Original indication drug | Ramucirumab | Ramucirumab |  |
| Repurposed Indication | Trypanosomiasis | Trypanosomiasis |  |
| Repurposed Indication Drug | Bortezomib, Dexamethasone | Bortezomib, Dexamethasone |  |
| **Drug name** | **Digoxin** | **Digoxin** | **Digoxin** |
| Cluster# | 20 | 3 | 3 |
| Original Indication | Congestive Heart Failure | Congestive Heart Failure | Congestive Heart Failure |
| Original indication drug | Atenolol | Atenolol | Atenolol |
| Repurposed Indication | Cancer | Cancer | Cancer |
| Repurposed Indication Drug | Digitoxin | Digitoxin | Digitoxin |

 **Supplementary Table 4. Repurposing suggestion details - Glyburide**

|  |  |  |
| --- | --- | --- |
|  | Hierarchical clustering | |
| Drug name: Glyburide | In silico Experiment 2 | In silico Experiment 3 |
| Cluster# | 14 (anti-diabetic) | 14 (anti-diabetic) |
| Original Indication | Diabetes | Diabetes |
| Original indication drug | Metformin, Pioglitazone | Metformin, Pioglitazone |
| Repurposed Indication | Heart Failure | Heart Failure |
| Repurposed Indication Drug | Diazoxide [37] | Diazoxide [37] |

**Supplementary Table 5.** **Repurposing suggestion details - Stanozolol**

|  |  |  |  |
| --- | --- | --- | --- |
|  | Hierarchical Clustering | | |
| Drug name: Stanozolol | In silico Experiment 1 | In silico Experiment 2 | In silico Experiment 3 |
| Cluster# | 11 (hormonal therapeutics) | 17 (hormonal therapeutics) | 9 (hormonal therapeutics) |
| Original Indication | Osteoporosis | Osteoporosis | Osteoporosis |
| Original indication drug | Estrogen, Raloxifene hydrochloride | Estrogen, Raloxifene hydrochloride | Estrogen, Raloxifene hydrochloride |
| Repurposed Indication | Hormone Sensitive Breast Cancer | Hormone Sensitive Breast Cancer | Hormone Sensitive Breast Cancer |
| Repurposed Indication Drug | Anastrozole and Exemestane | Anastrozole and Exemestane | Anastrozole and Exemestane |

**Supplementary Table 6.** **Repurposing suggestion details - Rimexolone**

|  |  |  |
| --- | --- | --- |
|  | Hierarchical Clustering | |
| Drug name: Rimexolone | In silico Experiment 1 | In silico Experiment 3 |
| Cluster# | 30 (ophthalmic medicines) | 26 (ophthalmic medicines) |
| Original Indication | Eye Inflammation (Uveitis) | Eye Inflammation (Uveitis) |
| Original indication drug | Fluorometholone [44] | Fluorometholone  [44] |
| Repurposed Indication | Eyelid Dermatitis | Eyelid Dermatitis |
| Repurposed Indication Drug | Fluprednisolone | Fluprednisolone |

**Supplementary Table 7.** **Repurposing suggestion details - Carbachol**

|  |  |  |
| --- | --- | --- |
|  | Hierarchical clustering | |
| Drug name: Carbachol | In silico Experiment 2 | In silico Experiment 3 |
| Cluster# | 6 (Neuronal agonists/antagonists) | 12 (Neuronal agonists/antagonists) |
| Original Indication | Glaucoma | Glaucoma |
| Original indication drug | Pilocarpine | Pilocarpine |
| Repurposed Indication | Anti-parasitic | Anti-parasitic |
| Repurposed Indication Drug | Capsaicin[49], Memantine[50] and Chlorpromazine [51] | Capsaicin[49], Memantine[50] and Chlorpromazine [51] |

**Supplementary Table 8.** **Repurposing suggestion details - Pilocarpine**

|  |  |  |
| --- | --- | --- |
|  | Hierarchical clustering | |
| Drug name: Pilocarpine | In silico Experiment 2 | In silico Experiment 3 |
| Cluster# | 6 (Neuronal agonists/antagonists) | 12 (Neuronal agonists/antagonists) |
| Original Indication | Glaucoma | Glaucoma |
| Original indication drug | Carbachol | Carbachol |
| Repurposed Indication | Anti-parasitic | Anti-parasitic |
| Repurposed Indication Drug | Capsaicin[49], Memantine[50] and Chlorpromazine [51] | Capsaicin[49], Memantine[50] and Chlorpromazine [51] |

**Supplementary Table 9.** **Repurposing suggestion details - Aminophylline**

|  |  |  |  |
| --- | --- | --- | --- |
|  | K-means clustering | | |
| Drug name: Aminophylline | In silico Experiment 1 | In silico Experiment 2 | In silico Experiment 3 |
| Cluster# | 3 [vasodilators and vasoconstrictors] | 3 [vasodilators and vasoconstrictors] | 3 [vasodilators and vasoconstrictors] |
| Original Indication | Asthma | Asthma | Asthma |
| Original indication drug | Theophylline, Iloprost | Theophylline, Iloprost | Iloprost |
| Repurposed Indication | Alzheimer’s | Alzheimer’s | Alzheimer’s |
| Repurposed Indication Drug | Nimodipine [55], Nicardipine[56, 57] and Ergoloid Mesylates [58] | Nimodipine [55], Nicardipine [56, 57] and Ergoloid Mesylates [58] | Nimodipine [55], Nicardipine[56, 57] and Ergoloid Mesylates [58] |

**Supplementary Table 10.** **Repurposing suggestion details - Theophylline**

|  |  |  |
| --- | --- | --- |
|  | K-means clustering | |
| Drug name: Theophylline | In silico Experiment 1 | In silico Experiment 2 |
| Cluster# | 3 [vasodilators and vasoconstrictors] | 3 [vasodilators and vasoconstrictors] |
| Original Indication | Asthma | Asthma |
| Original indication drug | Aminophylline, Iloprost | Aminophylline, Iloprost |
| Repurposed Indication | Alzheimer’s | Alzheimer’s |
| Repurposed Indication Drug | Nimodipine [55], Nicardipine[56, 57] and Ergoloid Mesylates [58] | Nimodipine [55], Nicardipine[56, 57] and Ergoloid Mesylates [58] |