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Editorial

Hattrick Top 2% Scientist at SLS: Dr. P. Ashokkumar D. MubarakAli

School of Life Sciences, B.S.Abdur Rahman Crescent Institute of Science and Technology,
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Standford University of the United states of America has recently released a list of top 2% of the most cited scientists in diverse academic disciplines. A total number of ~160K professionals were enlisted from all over the world. Out of which approximately 1.5K scienstist are Indians representing varied institions. This database included the top 2% of scientists of the world. The results so obtained have been seggregated into 22 scientific area and 176 sub areas recently published in the Elsevier. Dr. P. Ashokkumar, Associate Professor in School of Life Sciences, B.S.Abdur Rahman Crescent Institute of Science and Technology, Chennai-600048, Tamil Nadu, India is one of them who got **113369** for his research accomplishment in the field of Cancer Biology. To celebrate his attainment, he was feliciated by Students of B.Tech Biotechnology wished and honored for his hattrick achivement for being Top 2% scientist for the years 2021, 2022 and 2023. Office bearers of SLS newsletter acknowleding his hard work and dedications towards research and publishing the content at the front article.



* Research Highlights

From first symptoms to diagnosis: Initial Clinical presentation of primary brain tumors

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Research Highlights

Despite modern imaging methods, long symptoms-to-diagnosis intervals can be observed in patients with primary brain tumors. A brain tumor is generally defined as growth of cells in brain or near it. It can happen in brain tissue. Brain tumors are classified into two types based on its severity. They are Primary brain tumor and Secondary brain tumor. Patients with primary brain tumors can experience generalized symptoms and most of them are focal depending on the localization of the lesion. This study mainly aims about primary brain tumors in which they evaluate the initial and subsequent clinical presentation of brain tumor in context to time to diagnosis, localization, histology and tumor grading.

Several studies on initial brain tumor symptoms on both children and adolescents were published. One of those studies reported that most of the adults are facing symptoms of malignant cerebral gliomas. Davies and clerk in of their interview mentioned that symptoms of treated patients with malignant cerebral gliomas and relatives reported more personality changes (30 vs 15%), cognitive loss (46 vs 33%) and fatigue (48 vs 14%). While some brain tumors are diagnosed quickly, symptom-to-diagnosis period takes at least 14 weeks . In an investigation it is reported that it took a median time of 65 days to diagnose the medulloblastomas in children. In order to understand symptoms and their relations with different factors, retrospective analysis was carried out.

Retrospective analysis of patients with brain tumor was performed based on their medical records. Information were collected based on age at time of diagnosis, sex, tumor type, histology ,WHO tumor grading ,their intial symptoms and subsequent clinical findings, interval. Further they classified symptoms as "first presenting symptom" and "symptoms developing over time". Further interval from first symptom to diagnosis (grade 1 vs grade 3-4) were analysed. Further statistical calculation was approached in order to calculate distribution. Normal distribution was calculated by Kolmogorov-Smirnov test. As parameter of symptom to diagnosis interval didn't show normal distribution, non parametric testing was used. Mean,Interquartile range standard deviations were given. The p -value >0.05 was considered to be significant. So for this, data of 85 patients were recorded (54 male and 31 female) ranging from 6 to 79 years. WHO grading were obtained in 72 patients. Using the data and mathematical calculations results were obtained. A total of 60% patients subjected to malignant tumour, 24.7% to benign tumor and 15.3% were not classified. Along with that 165 signs were found and listed in descending order which includes epileptic seizures, headaches, sensory disturbances, cognitive impairment, ataxia and visual disturbances nausea. These were the initial symptoms of the patients. Later it was noticed that there is an increase in severity of the above mentioned symptoms along with which aphasia, motor weakness, appetite loss were also observed.

Apart from these symptomatic epilepsy such as Astrocytic tumors(42.4%), Oligodendrogliomas and Mixed gliomas(12.9%), Embryonic tumors (4.7%), Meningiomas (4.7%) were commonly observed in some patients. To understand the difference between symptom to diagnosis interval of low and high grade tumors results of 72 patients were obtained. The results included that Grade 1 had longest symptom to diagnosis interval (N=6) with mean of 232 days, followed by Grade 2 tumors with 138 days (N=15). For Grade 4 (N=14) and Grade 4 (N=37). High grade tumors were diagnosed faster than low grade tumors. Grade 3 and Grade 4 were diagnosed faster than Grade 2 median:26 vs 138 days; z= -3.847,(p smaller than 0.01) Additionally localization with respect to symptoms were also observed. It was found that 21% of tumors were localized frontally, 17.6% were temporal, 10.6% were parieto-occupital and 12.9% in cerebellum.

Finally from the above information, it helps us to know about the frequency of initial and subsequent symptoms of primary brain tumor until diagnosis in relation with time to diagnosis

and tumor pathology of patients treated at Department of Neurology at University Hospital in Zurich from 2005 to 2010. It is also observed that occurrence of headache did not differ between low and high grade tumor. Brain scan cannot be suggested for every symptoms. Hence SNOOP10 criteria can be carried out for red flags and diagnostic workshops can be conducted related to SNOOP10 criteria so that it can be easy for quicker diagnosis. Studies support these ideas as it helps them to diagnose quicker.

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Mini Review

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Effect of Botulinum Toxin A on Proliferation and Apoptosis in the T47D Breast Cancer Cell Line

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Research highlight:

Women breast cancer is the major health problem worldwide. In 2022 2.3 million women were diagnosed with breast cancer. It is a heterogeneous disease; different treatments include surgeries like lumpectomy and mastectomy, radiation therapy, chemotherapy, hormone therapy, immunotherapy etc... Widely used botulinum toxin A derived from bacterium Clostridium botulinum is used for its effect on relaxing skeletal muscles, also inhibits the growth of cancer cells in dose-dependent manner. This study was performed to investigate the effect of BtxA on T47D cancer cell proliferation and apoptosis. MCF10A nontumoral cell line and T47D cancer cell lines were both cultured in DMEM/F-2 medium and RPMI-1640 medium respectively provided with growth factors, antibodies etc. BtxA per vial of 100 units/allergan solution in 0.9% saline is used. MTT [3-(4,5-dimethylthiazol-2-yl)-2,5diphenyltetrazolium bromide] Assay was performed to check the cell viability of T47D cells using BtxA. In this assay cells treated with different concentrations of BtxA is incubated for 24h. Then they are washed twice with PBS buffer solution incubated again for 30 minutes at 37°C leading to formation of crystals which are dissolved using dimethyl sulfoxide. As a result there was a significant inhibitory effect on proliferation and BtxA has cytotoxic effects on cancer cell lines. There was a reduced IC50 value.

Morphological changes were studied where the cells were treated with BtxA of different concentrations and untreated cells were used as negative control. Cells were observed in normal inverted microscope 24h post treatment. When observed cells were detached from monolayer

and were rounded up. Cells possessed condensed chromatin, displayed membrane shrinkage and were granulated and vaculated. FACS (Fluorescence activated cell sorting) is carried out to determine the effect of BtxA. PI and PI/Annexin V staining is done to check the cell viability and distinguish between between apoptosis and necrosis. For Propidium idodide (PI) cells attached in 6-well plates were treated with BtxA in time intervals. Then these cells were harvested and washed in PBS, fixed in iced-ethanol and stored on -20°C. For further analysis, cells were washed in PBS and suspended in PI(25mg/mL) in PBS with RNase A. For PI/Annexin V double staining cells were harvested and suspended in binding buffer (HEPES- N-2-hydroxyethylpiperazine-N-2ethane sulfonic acid). Further group of cells were incubated for 15 minutes with Annexin V FITC and PI. Flow cytometry analysis was carried out. In consequence of double staining it was revealed that BtxA acts very fast . Both T47D and MCF 10 A showed pre-apoptotic subpopulation, apoptotic sub-population and necrotic sub-population. Caspase is a family of cysteinyl aspartate-specific proteases involved in apoptosis. Caspase-Glo 3/7 kit was used to analyse the effect of BtxA on Caspase 3/7 activity in T47D cell lines where cells cultured in PRMI is treated with BtxA IC50 or DMSO. Caspase 3/7 reagent was added after 24h, mixed well and incubated for 1h at room temperature. It was noticed that caspase-3 activity in cancer cell was 14 fold higher than that of non-tumoral cells. It is shown that BtxA mediate apoptosis. In most cases cancer treatment involves use of cytotoxic agents such as doxorubicin, bleomycin and cisplatin which are harmful and very costly. As an alternative, this study was conducted to know the effect of BtxA on cancer cells which is cytotoxic in time-dependent and dose-dependent manner. At high concentrations of BtxA there was a significant decrease in cell viability. Hence BtxA can be used as an alternative treatment for breast cancer.

For Further Reading: Cindy Bandala, Jose Luis Martin Perez-Santos, Eleazar Lara-Padilla, Ma. Guadalupe Delgado Lopez, Maricruz Anaya-Ruiz.2013, Effect of Botulinum Toxin A on Proliferation and Apoptosis in the T47D Breast Cancer Cell Line. Asian pacific J Cancer prev,14(2),891-894.

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Mini Review

Kidney and Lung Transplantation in India

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Introduction:

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Transplantation is a medical procedure in which an organ or a tissue is transferred from one person (Donor) to another person (Recipient) or from one area of a person's body to another area. Generally, there are four types of transplantation: Autograft (Between the same individual), Isograft (Between identical twins), Allograft (Between two individuals of the same species), and Xenograft (Between two different species). Kidney and lung transplantation mostly comes under isograft and allograft. Xenograft of kidney and lung is possible but till today there is no successful transplant in patients with a long-term survival rate.

Kidney Transplantation:

Kidney transplantation is the best cost-effective renal replacement therapy option for patients with end-stage kidney disease. Kidney transplantation has shown better long-term survival rates than dialysis. In India, most kidney transplants are from living donors (80% to 90%) and few are from deceased donors (10% to 20%). Gujarat, Tamil Nadu, Telangana, Maharashtra, Kerala, Chandigarh, and Karnataka are states in India with active deceased donor kidney transplant in the past ten years. Institute of Kidney Diseases and Research Center, Dr. H. L. Trivedi Institute of Transplantation Sciences (IKDRC-ITS) is the largest public-sector transplant hospital in India located in Ahmedabad, Gujarat.

Cost of Transplant in IKDRC-ITS

Transplantation and follow-up treatment in IKDRC-ITS is free for all children in the Gujarat Government School Health program, and also for patients below the poverty line and

from scheduled castes and tribes, and farmers. Subsidized treatment is provided free in IKDRC-ITS for all other patients, as required. The cost of kidney transplant in IKDRC-ITS is USD 5000. The generic maintenance immunosuppressive drugs are around 50% cheaper for public sector hospitals than private sector hospitals in India.

Results reported by GODT and IKDRC-ITS

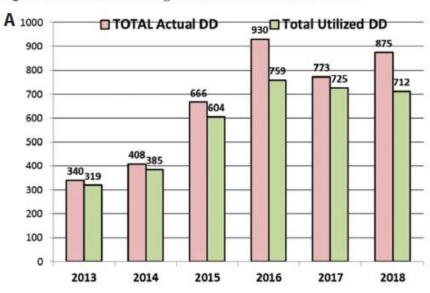
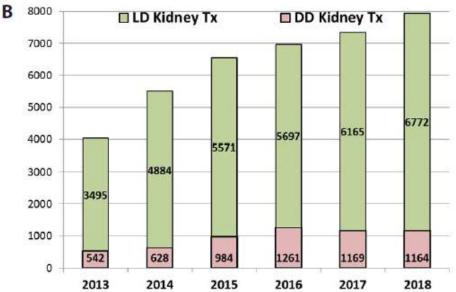


Figure 1. Deceased-Donor Organ Donation in India: 2013 to 2018



The total numbers of deceased organ donors in India from 2010 to 2018 are shown in figure 1 and from 2013 to 2018 in figure 1 A. Living Donor (LD) and Deceased Donor (DD) kidney transplants in India from 2013 to 2018 are shown in figure B.

Deceased Donor Kidney Transplants (DDKT) and Living Donor Kidney Transplants (LDKT) data reported by IKDRC-ITS from January 1997 to March 2020 are shown in figures 2 and 3 respectively.

IKDRC-ITS transplant data from January 1997 to March 2020 is shown in table 1.

Table 1. Institute of Kidney Diseases and Research Center, Dr. H. L. Trivedi Institute of Transplantation Sciences, Ahmedabad, India: Transplant Data From January 1, 1997 to March 15, 2020

Year	LDKT	DDKT	KPD	Total KT	DDLT	LDLT
1997	54	6	0	60	0	0
1998	126	8	0	134	0	0
1999	156	9	0	165	0	0
2000	153	11	4	164	0	0
2001	135	21	2	156	0	0
2002	105	9	0	114	0	0
2003	140	10	4	150	0	
2004	146	11	0	157	0	0
2005	129	21	4	150	0	0
2006	186	45	2	231	0	0
2007	246	32	4	278	0	0
2008	234	38	4	272	2	0
2009	283	45	10	328	8	0
2010	233	42	8	275	14	0
2011	215	45	14	260	14	0
2012	291	26	28	317	14	0
2013	355	45	56	400	20	0
2014	309	39	56	348	22	0
2015	307	71	75	378	36	6
2016	238	103	42	341	54	5
2017	239	106	29	345	63	6 5 1
2018	256	94	33	350	49	9
2019	303	87	48	390	52	16
2020 ^a	56	19	17	75	13	1
Total	4895	943	440	5838	361	39

Figure 1. Total Numbers of Actual Deceased Organ Donors in India: 2010-2018

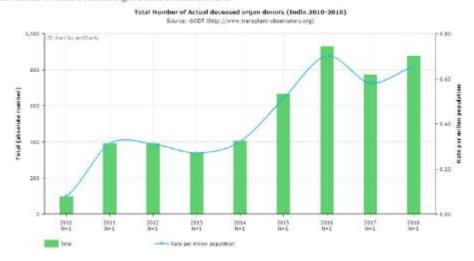


Figure 2. Institute of Kidney Diseases and Research Center, Dr. H. L. Trivedi Institute of Transplantation Sciences, Ahmedabad, India: Deceased Donor Kidney Transplants From January 1, 1997 to March 15, 2020

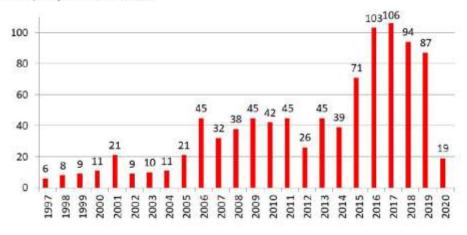


Figure 3. Institute of Kidney Diseases and Research Center, Dr. H. L. Trivedi Institute of Transplantation Sciences, Ahmedabad, India: Living Donor Kidney Transplants From January 1, 1997 to March 15, 2020



The first successful living donor kidney transplant in India was performed in 1984 and the first successful deceased donor kidney transplant in India from donation after cardiac death was performed in 1987 by Dr. H. L. Trivedi, founder-director of IKDRC-ITS. Including 4895 LDKT, 5838 943 DDKT, and 440 living donor paired donation transplants, a total of kidnev transplants were completed by IKDRC-ITS. Mean recipient and donor ages were 38 ± 14 years and 45.3 ± 17.13 years respectively. Donors with brain death due to cerebrovascular accidents, comorbid conditions such as hypertension and diabetes, and road traffic accidents were a majority of donors. Chronic glomerulonephritis, diabetes, hypertension, end-stage kidney disease due to unknown etiology, autosomal-dependent polycystic kidney disease, glomerular diseases, obstructive uropathy, single-unit kidney, and retransplant were the most common diseases that may lead to end-stage kidney disease in recipients. The patient survival rate was 70%, and the death-censored graft survival rate was 84% with a mean follow-up time of 8 ± 5.4 years. 25% of the patients had shown delayed graft function and 21% of the patients showed biopsy-proven acute rejection.

Lung Transplantation

For select progressive end-stage lung disease patients, Lung transplantation is the definitive treatment despite being on optimum medical therapy. In Humans, the first lung transplantation was attempted by James Hardy in 1963. The first successful lung transplantation was reported by Joel Cooper in 1983.

Origin of Lung Transplantation in India

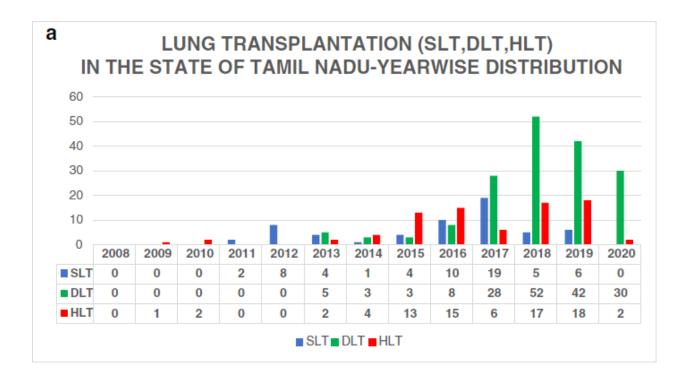
In India, the first double-lung transplantation (DLT) and first combined heart-lung transplantation (HLT) were performed by Dr. KM Cherian in 1999. After this, there was a decline in Lung transplantation, until 2007, when Apollo Hospitals, Chennai performed combined heart-lung transplantation. Single lung transplantation (SLT) was performed by Global Hospitals, Chennai in 2011. In Maharashtra, the first SLT was performed by Hinduja Hospital, Mumbai in July 2012. In Telangana, the first SLT was performed by Yashoda Hospital in September 2012. In Rajasthan, the first combined HLT was performed by Mahatma Gandhi Hospital, Jaipur in December 2016. In Kerala, the first combined HLT was performed by Lissie Hospital, Kochi in

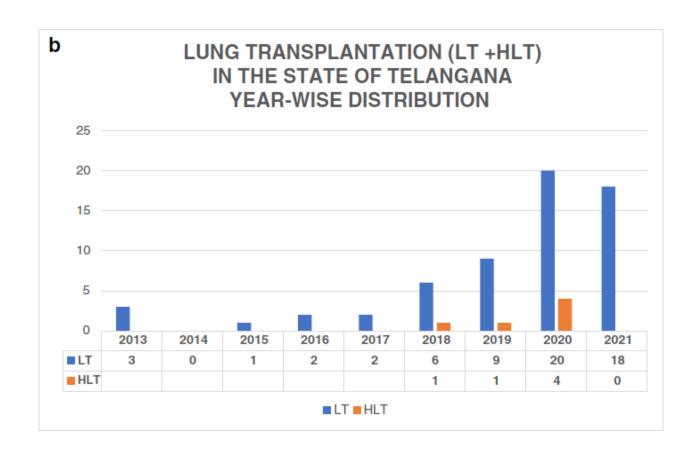
January 2016. In Karnataka, the first DLT in June 2018 and the first combined HLT in January 2019 were performed by Narayana Hrudayala Hospital, Bengaluru.

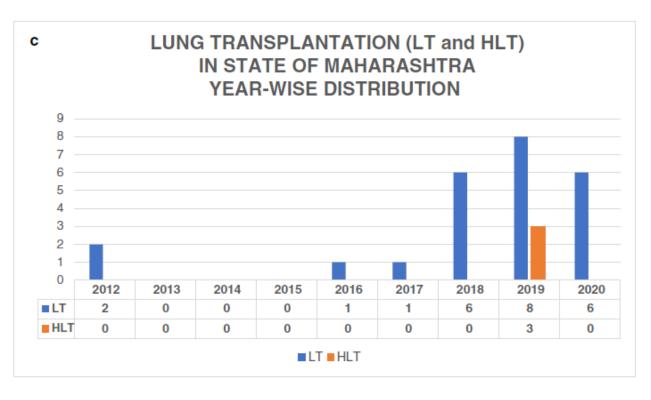
Characteristics of an Ideal Donor

- Age less than 55 years
- Clear Chest Radiography
- pO₂ more than 400 mmHg on 100% oxygen with positive end-expiratory pressure of 5-8 cm water
- Less than 20 pack-year smoking history
- Absence of chest trauma
- No signs of aspiration or sepsis
- Sputum or endotracheal tube aspirate negative for bacteria on Gram stain
- Normal bronchoscopy without significant secretions

Reports of Lung Transplantation in India

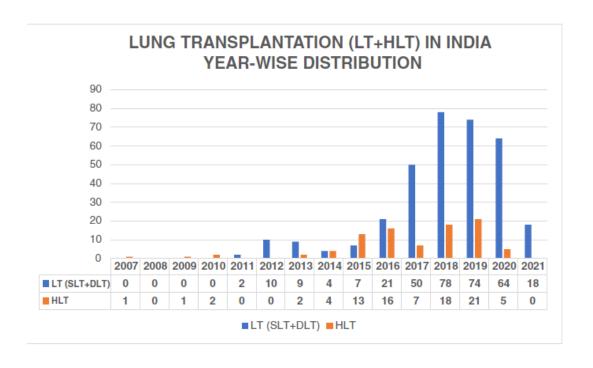






In India, 5 states and 1 UT have centres for performing isolated LT and combined HLT. 339 isolated LTs have been performed in Tamil Nadu, Telangana, Karnataka, Maharashtra, Punjab, and Delhi and 102 combined HLTs have been performed in Tamil Nadu, Telangana, Kerala, Karnataka, Maharashtra, and Rajasthan. In Tamil Nadu, a total of 257 isolated LTs and 83 combined HLTs have been performed. Of which 252 isolated LTs and all the 83 combined HLTs were performed in Chennai and 5 isolated LTs were performed in Coimbatore. The chart depicting the number of LTs performed in Tamil Nadu is shown in figure a. In Telangana, 38 isolated LTs and 7 combined HLTs were performed in Hyderabad and Secundarabad. The chart depicting the number of LTs performed in Telangana from 2013 to 2021 is shown in figure b.

In Maharashtra, a total of 24 isolated LTs and 6 combined HLTs were performed in Mumbai. The chart depicting the number of LTs performed in Maharashtra from 2012 to 2020 is shown in figure c. In Karnataka, a total of 27 isolated LTs and 2 combined HLTs were performed in Bengaluru. In Delhi, one isolated LT was performed and in Kerala and Rajasthan, one combined HLT was performed in each state. The chart depicting the number of LTs in the whole of India is shown in figure 5.



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An Overview of STARTUP INDIA

Mr. Jeno Andro Nicus, X.

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Startup India is a flagship programme of the Indian government that aims to create an effective open ecosystem for innovation and entrepreneurship in India. The Startup India Initiative was established on January 16, 2016, and since then, it has implemented a number of programs aimed at assisting entrepreneurs, developing a strong startup ecosystem, and changing India so that job creators rather than job seekers dominate the nation. These programs are managed by a dedicated Startup India Team, which reports to the Department for Industrial Policy and Promotion (DPIIT).

Recognition:

Eligible businesses can apply to be recognized by DPIIT as Startups under the Startup India initiative, which grants them access to a number of tax benefits like tax exemption, simpler compliance, IPR fast-tracking, and various other benefits.



Eligibility Criteria for Startup Recognition:

- The Startup should be incorporated as a private limited company or registered as a partnership firm or a limited liability partnership
- Turnover should be less than INR 100 Crores in any of the previous financial years
- The Startup should be working towards innovation/ improvement of existing products, services and processes and should have the potential to generate employment/ create wealth. An entity formed by splitting up or reconstruction of an existing business shall not be considered a "Startup"
- An entity shall be considered as a startup up to 10 years from the date of its incorporation.

Funding:

Startup india facilitates the development of startups by enabling easier contact between startup entities and investors .The schemes and facilities provided are :

- Startup India Seed Fund Scheme (SISFS): This scheme aims to provide financial assistance to startups for proof of concept, prototype development, product trials, market entry and commercialization. This would enable these startups to graduate to a level where they will be able to raise investments from angel investors or venture capitalists or seek loans from commercial banks or financial institutions.
- **Startup India Investor Connect:** This serves as a platform that connects startups with investors to facilitate investment opportunities through AI based matchmaking. Through this, entrepreneurs will be able to directly reach out to multiple investors using one single application and pitch their startup idea.
- Credit Guarantee Scheme for Startups: The Government of India established the Credit Guarantee Scheme, that provides startups a credit guarantee, with a fixed corpus to loans extended to DPIIT recognized startups by Scheduled Commercial Banks, Non-Banking Financial Companies (NBFCs) and Venture Debt Funds (VDFs) under SEBI registered Alternative Investment Funds.

Schemes:

Startup india provides several schemes that support the growth of indian startups. The government recognizes the importance of startups in driving innovation and economic growth. Various ministries and departments have introduced schemes to provide financial, infrastructural, and regulatory support to startups.

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The listed schemes cover sectors like technology, manufacturing, agriculture, healthcare, and more. The schemes include Central government schemes and women entrepreneurship schemes. The Central Government Schemes section serves as a valuable resource for entrepreneurs to explore government support measures.

Some of the schemes are Small Business Innovation Research Initiative (SBIRI), Technology Development Programme, Extra Mural Research Funding, Assistance to Professional Bodies & Seminars/ Symposia, Biotechnology Ignition Grant, Biotechnology Industry Partnership Program (BIPP), Research & Development in Processed Food, Agro Processing Cluster Scheme, Venture Capital Assistance Scheme and many more.

Initiatives:

- National Startup Awards 2023
- States Startup Ranking
- National Startup Awards
- Shanghai Cooperation Organization (SCO) Startup Forum
- Startup India Yatra
- Startup India Seed Fund Scheme
- MAARG Mentorship Platform
- Startup India Investor Connect



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Resources:

There are various resources provided by startup india that helps entrepreneurs to establish a startup hassle free. The resources include: Online courses, Market research reports, Patent facilitation, Trademark facilitation, Startup idea bank

Market access:

Procurement by Government:

Startups canbid for government tenders and become a seller to the Government through the Government e-Marketplace(GeM) and other channels.

International connectivity:

India has startup bridges with many countries ,that facilitates startups to connect with the startups of other countries and enables collaboration between them . By this the market of the startup can be expanded globally. startup bridges of india include:

- India Saudi Startup Bridge
- India Taiwan Startup Bridge
- India Bangladesh Startup Bridge
- India Italy Startup Bridge
- India Switzerland Startup Bridge
- India Qatar Startup Bridge

- India UAE Startup Bridge
- India Canada Startup Bridge
- India Croatia Startup Bridge
- India Finland Startup Hub
- India Brazil Startup Bridge
- UK-India Startup Launchpad
- Indo-Russian Innovation Bridge
- India Korea Startup hub
- Japan India Startup Hub
- India Portugal Startup Hub
- Sweden India Startup Sambandh Hub

Startup Toolkits & Facilities

A plethora of resources and information guides for you to propel in your entrepreneurial journey, basis your current stage. For some of these resources, you may be asked to register on the Startup India portal.



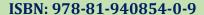
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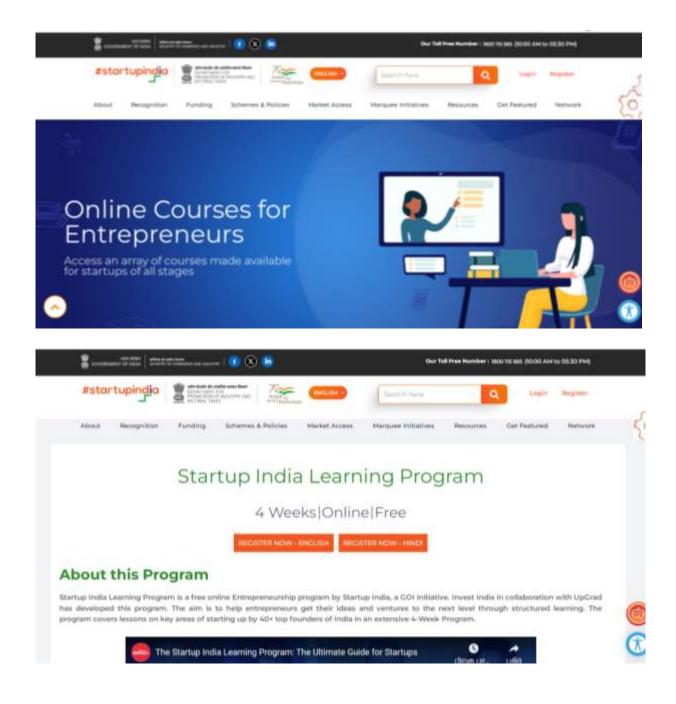
Where the entrepreneur has an interesting idea and is working on bringing it to life.

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