

Selling Stem Cells in the USA: Assessing the Direct-to-Consumer Industry

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Direct-to-consumer marketing of unapproved stem cell interventions is a well-known phenomenon in countries with lax medical regulations. However, an examination of Internet-based marketing claims revealed widespread promotion of such interventions by businesses based in the United States. Such commercial activity suggests that regulatory agencies must better oversee this marketplace.

Businesses marketing putative stem cell interventions have proliferated across the U.S. This commercial activity generates a host of serious ethical, scientific, legal, regulatory, and policy concerns. Perhaps the most obvious regulatory question is whether businesses advertising nonhomologous autologous, allogeneic, “induced pluripotent,” or xenogeneic “stem cell therapies” are exposing their clients to noncompliant cell-based interventions. Such practices also prompt ethical concerns about the safety and efficacy of marketed interventions, accuracy in advertising, the quality of informed consent, and the exposure of vulnerable individuals to unjustifiable risks.

Prior analyses of companies engaged in direct-to-consumer marketing of stem cell interventions have not explicitly focused on attempting to comprehensively locate and examine U.S. businesses (Lau et al., 2008; Ogbogu et al., 2013; Regenberg et al., 2009), although recent scholarship has identified some U.S. businesses engaged in such activity (Connolly et al., 2014). While such companies have attracted some scrutiny from researchers and journalists, these businesses have not yet been examined in a comprehensive manner (Perrone, 2015; Turner 2015a). This gap in scholarship has contributed to misunderstandings that need to be corrected.

For example, health researchers, policy-makers, patient advocacy groups, and reporters often use the phrase “stem cell tourism” when addressing the subject of unapproved cell-based interventions and even in 2016 assume that U.S. citizens must travel to such

destinations as China, India, Mexico, and the Caribbean if they wish to access businesses promoting stem cell procedures for a wide range of clinical indications. While travel from the U.S. to international “stem cell clinics” continues, the rhetoric of “stem cell tourism” often fails to acknowledge the hundreds of U.S. businesses engaged in direct-to-consumer advertising of stem cell interventions.

To address the urgent need for better information concerning the U.S. marketplace for such businesses, we used Internet key word searches, text mining, and content analysis of company websites to investigate and analyze this arena. We used key words and phrases such as “stem cell treatment” and “stem cell therapy” to find putative stem cell businesses and then evaluated the text on each given site to refine our analysis. Here we discuss the variety and prevalence of different kinds of stem cell interventions currently advertised and the breadth of marketing claims that U.S. businesses make. Our analysis should be useful to health researchers, policy-makers, regulators, patients and their advocates, and other parties.

Geographic Locations and Distribution of U.S. Businesses Marketing Stem Cell Interventions

Using rigorous Internet-based key word searches (see *Supplemental Information* for details), we found 351 U.S. businesses engaged in direct-to-consumer marketing of stem cell interventions offered at 570 clinics. For each business, we collected the company name,

location(s), website address, advertised stem cell types, and diseases, injuries, and other conditions that clinics claim to treat with stem cell interventions. (Table S1 lists and describes all of the businesses we identified).

Figure 1 shows the geographic distribution of such businesses across the U.S. Many stem cell companies employ multiple physicians and advertise interventions available at numerous clinics. Although such businesses are widely distributed all over the country, we found that clinics tend to cluster in particular states. For example, we found 113 clinics in California, 104 in Florida, 71 in Texas, 37 in Colorado, 36 in Arizona, and 21 in New York. “Hotspot” cities including Beverly Hills (18), New York (14), San Antonio (13), Los Angeles (12), Austin (11), Scottsdale (11), and Phoenix (10) are designated with stars on the map. Some metropolitan areas, including Southern California around Los Angeles and San Diego, the South Florida region surrounding Miami, the greater Denver area, and the Dallas-Fort Worth metro region, have a relatively high number of clinics even if not all such facilities are technically in one city (Figure S1). While our analyses here do not explain why these businesses cluster in particular areas, we plan to investigate this question further. Possible factors include a relationship between number of clinics and population density, regional variations in use of “alternative” medical interventions, aging population demographics, and regulatory orientation of state medical boards and consumer protection agencies.

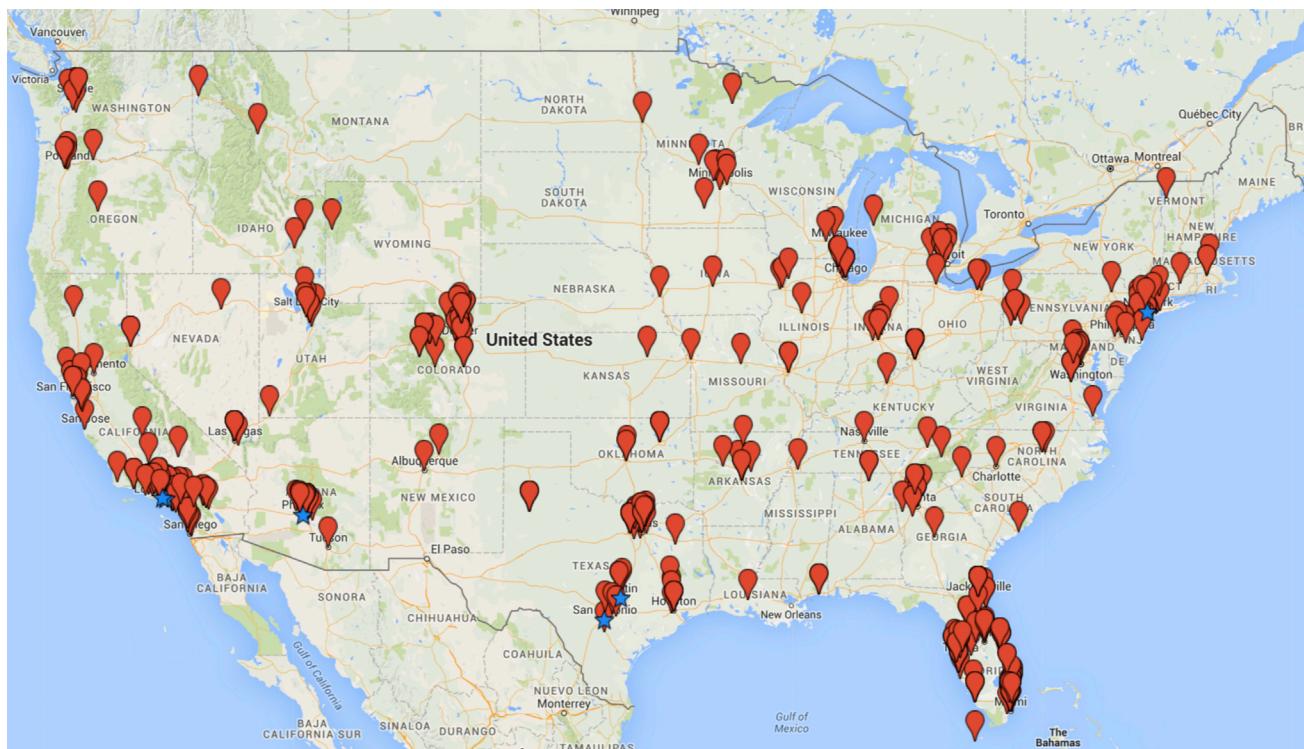


Figure 1. Map of Locations of Included Businesses

We conducted data collection on the cities and states of stem cell businesses including multiple locations for individual businesses. "Hotspot" cities are indicated with blue stars. See [Supplemental Information](#) for additional details concerning the production of the map.

Types of Advertised Stem Cell Interventions

We also analyzed the particular stem cell types that businesses advertise (Figure 2A). Most of the businesses we identified market autologous cell-based interventions, with an estimated one in five advertising allogeneic stem cell interventions sourced from amniotic material (17%), placental tissue (3.4%), and umbilical cords (0.6%). Some clinics market both autologous and allogeneic stem cells.

Of the businesses advertising autologous stem cell procedures, 61% market autologous adipose-derived stem cell-based interventions, 48% market what they describe as autologous stem cells obtained from bone marrow, and 4% market stem cells reportedly obtained from peripheral blood. Adipose stem cells were most often referred to using the adjective "adipose," but some companies used phrases such as "fat stem cells" and other businesses advertised that they use "stromal vascular fraction" or "SVF." Bone marrow stem cells were also sometimes referred to as "bone marrow aspirate concentrate" or

"BMAC." Combinations of stem cell types were also promoted. We found that a mixture of autologous adipose and bone marrow stem cells is the most commonly advertised "combination stem cell therapy."

Clinics marketing amniotic stem cells, amniotic stem cell allografts, or amniotic stem cell fluid also sometimes used such terms as "placenta" or "placental stem cells." The relative abundance of U.S. businesses marketing "amniotic" and "placental" stem cells was notable. The precise source of these products is not clear in all cases, particularly for allogeneic products such as amniotic stem cells.

One business promotes access to what it claims are induced pluripotent stem cells. This company did not indicate the purported source of induced pluripotent stem cells or address whether they are derived on a patient-by-patient basis for autologous therapy. Another business markets access to what it describes as "embryonic stem cell" interventions. In addition, we identified two clinics that marketed "bovine amniotic cells," a

xenogeneic product, for use in humans. Approximately 3% of businesses marketed stem cell interventions without mentioning a particular type of stem cells.

One unanticipated interpretive challenge we encountered is that many businesses advertise both stem cell interventions and platelet rich plasma (PRP) procedures either as the basis for separate treatments or as combination "cell therapies." Though not an actual stem cell product, PRP is sometimes marketed as an autologous "stem cell treatment" derived from peripheral blood. In such cases, the rhetoric of "stem cells" is presumably used as a marketing hook intended to attract potential customers (Turner, 2015b). For the purpose of our analysis, clinics marketing putative stem cell interventions derived from peripheral blood were included within the scope of our inquiry but clinics only marketing PRP interventions were excluded.

Marketing Claims about Clinical Indications

U.S. businesses promoting stem cell interventions claim to treat a wide range of

diseases and injuries, as well as advertising stem cells for cosmetic applications, “anti-aging,” and other purposes (Figure 2B). Some clinics occupy relatively specialized marketplace niches. For example, many cosmetic surgery clinics advertise such procedures as “stem cell facelifts” and “stem cell breast augmentation” as well as sexual enhancement procedures. Orthopedic and sports medicine clinics often promote stem cell interventions for joints and soft tissue injuries. Other clinics take a much broader approach and list stem cell interventions for 30 or more diseases and injuries. Such businesses commonly market treatments for neurological disorders and other degenerative conditions, spinal cord injuries, immunological conditions, cardiac diseases, pulmonary disorders, ophthalmological diseases and injuries, and urological diseases as well as cosmetic indications. Many of these marketing claims raise significant ethical issues given the lack of peer-reviewed evidence that advertised stem cell interventions are safe and efficacious for the treatment of particular diseases. Such promotional claims also generate regulatory concerns due to apparent noncompliance with federal regulations.

We also examined the prevalence of stem cell marketing claims targeted at parents or guardians of minors. We found nine clinics each promoting stem cells for autism and for cerebral palsy. We also identified 33 marketing claims for muscular dystrophy (MD), a disease that primarily though not exclusively afflicts children. This kind of advertising reveals another tangled knot of ethical and legal concerns, as the apparent target audience for such marketed interventions is not adults with decision-making capacity but rather the parents or guardians of children. A comparable kind of marketing situation may exist for Alzheimer’s disease (27 promoted claims) and other neurode-

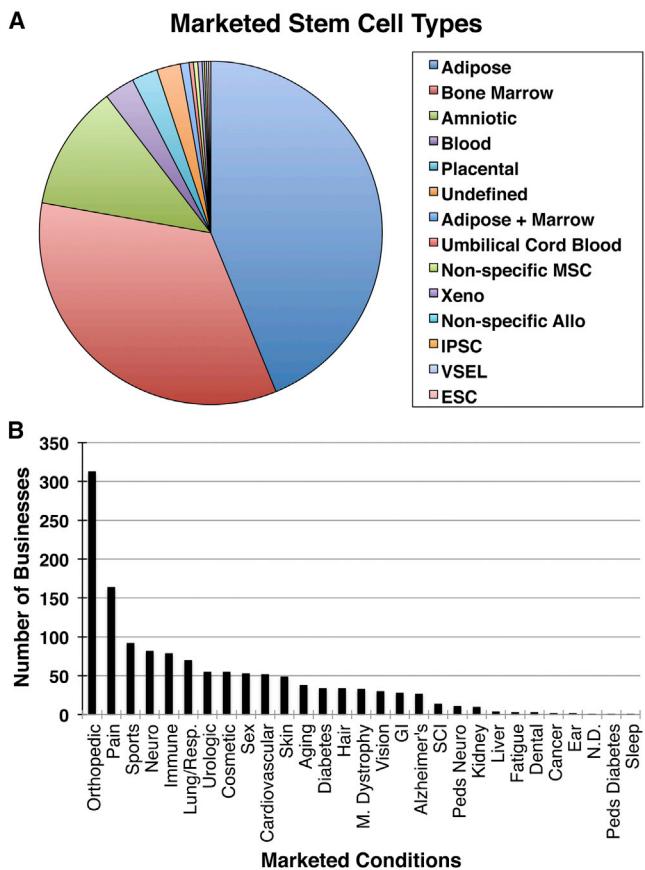


Figure 2. Stem Cell Types and Conditions Marketed
Data from stem cell business websites were collected and analyzed for claims related to the use of (A) specific types of stem cells marketed for (B) a range of conditions.

generative illnesses where in at least some cases patients themselves are not necessarily the primary targets of online advertising.

Ethical, Regulatory, and Policy Concerns

Our investigation was in part motivated by ethical, scientific, and regulatory concerns related to the proliferation of U.S. businesses engaged in direct-to-consumer marketing of stem cell interventions. However, it was not our intention to make evaluative statements concerning whether particular companies are marketing stem cell interventions in compliance with federal and state regulations as well as contemporary ethical standards for medical practice. Nor was it our intention to make ethical or legal assertions about specific marketing claims. We also did not address whether contemporary ethical, scientific, and legal

standards are being met by individual businesses. However, at a broader level we recognize the importance of these ethical issues and regulatory concerns (Knoepfle, 2015).

Given that many of the businesses we identified market autologous interventions that do not appear to fit FDA criteria for homologous use and minimal manipulation of cells and tissues, allogeneic products, combination products, or “xenogeneic stem cells,” there are clear grounds for concern that some of the companies we found are not compliant with federal regulations. There are related ethical concerns about information provided to prospective clients and the veracity of marketing claims, the safety and efficacy of advertised procedures, and the risk of physical, emotional, and financial harm to already ill or injured and vulnerable individuals. Recent draft guides issued by the FDA provide increased clarity concerning how the FDA interprets federal regulations applicable to the use,

sale, and distribution of stem cell products. These draft guidance documents suggest to some observers that the FDA is preparing to take increased regulatory action (<https://www.statnews.com/2016/02/08/fda-crackdown-stem-cell-clinics/>) in response to businesses selling stem cell interventions in a manner that some critics have described as exhibiting a “Cowboy Culture” (<http://www.nature.com/news/stem-cells-in-texas-cowboy-culture-1.12404>).

Some proponents of deregulation argue that current federal regulations governing the advertising, processing, and administration of autologous stem cells are too onerous and have resulted in few approved stem cell therapies reaching the American marketplace (Chirba and Garfield, 2011; McAllister et al., 2012). The REGROW Act is an example of the current push from some political quarters and even from some

individual stem cell researchers for lowering safety and efficacy standards for adult stem cell-based interventions. However, we found that hundreds of U.S. businesses are already promoting stem cell interventions for an extraordinary range of clinical indications. Advocates of deregulation will perhaps be pleased by our findings that many putative stem cell interventions are currently available for sale in the U.S. In contrast, proponents of a marketplace in which cell-based therapies have traditionally been tested for safety and efficacy and subject to pre-marketing review by the FDA will likely be concerned by how many U.S. businesses are currently marketing stem cell interventions. We are particularly concerned that we found many advertising claims related to ALS, Alzheimer's disease, Parkinson's disease, and many other conditions for which there is no established scientific consensus that proven safe and efficacious stem cell treatments now exist.

Given that we identified 351 businesses actively advertising stem cell products in the U.S., it is fair to ask whether regulatory inaction has emboldened entrepreneurial physicians and other market participants. We place a high value on the imperative to provide patients with safe and efficacious interventions and see a need for more effective regulation of the U.S. marketplace for stem cell interventions. Our analysis should serve as a valuable resource for contemporary debate concerning whether the U.S. marketplace for stem cell interventions is adequately monitored and regulated by the FDA, the Federal Trade Commission, state medical boards, and other agencies tasked with promoting patient safety and accurate advertising (<https://www.federalregister.gov/articles/2015/10/30/2015-27703/draft-guidances-relating-to-the-regulation-of-human-cells-tissues-or-cellular-or-tissue-based>).

[2015-27703/draft-guidances-relating-to-the-regulation-of-human-cells-tissues-or-cellular-or-tissue-based](https://www.federalregister.gov/articles/2015/10/30/2015-27703/draft-guidances-relating-to-the-regulation-of-human-cells-tissues-or-cellular-or-tissue-based)).

Weighing Risks and Benefits Associated with Identifying Marketing Stem Cell Interventions

While examining the U.S. marketplace for direct-to-consumer advertising of stem cell interventions, we gave careful consideration to possible risks associated with identifying and documenting specific businesses engaged in such commercial activity. We acknowledge that a public record containing locations and websites of businesses marketing stem cell interventions could be misappropriated and misused for marketing purposes, be used as a search tool by patients seeking particular procedures, or even be used to claim that, with so many businesses already operating in the U.S., de facto deregulation has occurred and it is too late for the FDA and other agencies to provide more robust regulatory oversight of this marketplace. While we recognize these risks, we argue that the benefits associated with a detailed examination of U.S. businesses marketing stem cell interventions outweigh potential risks. We also want to emphasize that we analyzed businesses that are already readily identifiable and take multiple steps to market their products. Patients have little difficulty finding stem cell clinics and comparable businesses on the Internet. The best way to address ethical, legal, and scientific issues related to such businesses is to acknowledge their existence, examine and evaluate their marketing claims, and conduct public debates and policy discussions in the most evidence-based manner possible.

SUPPLEMENTAL INFORMATION

Supplemental Information for this article includes investigation methods, one figure, and one table and can be found with this article online at [http://dx.doi.org/10.1016/j.stem.2016.06.007](https://dx.doi.org/10.1016/j.stem.2016.06.007).

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Supplemental Information

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Supplemental Information

Search approach

We used rigorous keyword-based Internet search methods, content analysis of company websites, and text mining to identify, analyze, and document U.S. businesses marketing stem cell interventions directly to consumers. Supplemental Table 1 lists individual companies and clinics as well as their websites, identifies their geographic locations, documents the type or types of stem cells clinics claim to use, notes particular stem cell procedures advertised, and, classifies specific interventions according to more general categories such as "neurological," "cardiopulmonary," "cosmetic," or "orthopedic." Diseases, injuries, and conditions for which stem cells were reportedly administered were recorded as they were listed on company websites. We maintained this approach even when company websites contained spelling errors or there were questions concerning the validity of the disease labels businesses used.

To identify U.S.-based businesses marketing stem cell interventions we conducted systematic Internet-based searches using the Google and Bing search engines. We also used Google Alerts to send us automatic alerts when businesses issued press releases, added new web content, posted videos, and attracted news coverage. In addition, we searched for companies on such sites as Facebook, Twitter, YouTube, and LinkedIn. For greater depth and because search tools can bring somewhat distinct results, we also conducted searches using different web browsers including Safari and Chrome.

During the process of trying to find U.S. businesses engaged in direct-to-consumer marketing of stem cell interventions we used search phrases such as "stem cell treatment" and "stem cell therapy" with accompanying terms such as "adipose", "amniotic", "bone marrow," and "placental." We also used search terms related to conditions and clinical specializations. For example, we used such terms as "orthopedic", "pain", and "arthritis". Our strategy was to search for businesses promoting stem cell interventions by using common marketing phrases. We also sought to use search terms that prospective clients might use when conducting Internet-based searches to find U.S. businesses marketing putative stem cell interventions. A comprehensive list of the search terms and phrases we used is provided starting on page 8 of this Supplemental Information document. In addition to the actual search results themselves, some clinics were identified by examining the advertisements that appeared accompanying search results. Other businesses were found by clicking every link on all reviewed search pages and examining each identified website.

In some cases we found individual businesses by searching for all clinics listed by such franchise operations as Cell Surgical Network and Regenexx. Searches for businesses named on such websites in some instances led to the specific types of affiliated clinics we were seeking and in other instances resulted in the

identification of new, previously unidentified U.S. companies marketing stem cell interventions.

When conducting Internet-based searches we reviewed anywhere from 15-25 pages of returns. We conducted shorter searches when search terms failed to identify new businesses. We proceeded further into returned pages when search terms continued to generate promising leads. We concluded searches when they stopped identifying previously unidentified U.S. businesses marketing stem cell interventions. This approach was based on the social science concept of saturation, in which the process of data gathering comes to an end when novel results or findings cease to be generated by a particular inquiry process.

The formal process of searching for businesses marketing stem cell interventions began September 1, 2015 and ended February 29, 2016. Before the formal search strategy commenced we were aware of numerous businesses now listed in the database. While the database is restricted to businesses that we identified on or before the end of February 2016, since that date we have noticed the emergence of additional U.S. companies engaged in direct-to-consumer marketing of stem cell interventions. Barring increased regulatory oversight of this marketplace, we anticipate that the number of such businesses will continue to grow through 2016 and beyond.

Inclusion and exclusion criteria used to identify U.S. businesses making internet-based direct-to-consumer marketing claims about stem cell interventions

To identify U.S. businesses specifically marketing stem cell interventions we used inclusion and exclusion criteria that helped us evaluate the many websites generated by Internet-based searches. Our objective was to find businesses that claim to be U.S.-based and promote access to stem cell interventions reportedly delivered within the U.S., engage in direct-to-consumer online marketing to prospective clients, and have websites that can be data-mined using the method of content analysis. We also restricted our search to businesses that appear to seek payment for putative stem cell interventions that have not received FDA pre-marketing approval in the form of approved New Drug Applications (NDA) or approved Biologics License applications (BLA) – as have some cord blood products – and were not providing access to cell-based interventions such as bone marrow transplants for various cancers and specific immunological disorders that are covered by many health insurers and fall within the scope of established medical practice. We excluded from our analysis businesses that market and administer stem cell interventions but indicate that they are based outside the U.S. Medical tourism facilitators and other businesses that are located in the U.S. but facilitate access to stem cell interventions provided outside the U.S. were also excluded from our database.

We also excluded from our analysis such entities as U.S. businesses and international companies engaged in mail order delivery of stem cell supplements, "neutraceuticals," and cosmetics; research facilities stating they conduct clinical trials with both institutional review board (IRB) approval and FDA-cleared Investigation New Drug applications (IND) or Investigational Device Exemptions (IDE); companies selling cell-processing medical devices to health care providers but not directly advertising stem cell interventions to prospective clients; and educational facilities and other institutions promoting courses and training related to stem cells.

Businesses advertising autologous bone marrow stem cell interventions were included in the list of companies provided in Supplemental Table 1. However, it should be noted that according to 21 CFR 1271.3 (d) (4), minimally manipulated bone marrow for homologous use does not require pre-marketing approval by the FDA. 21 CFR 1271.15 (b) states that facilities removing cells or tissues from an individual and implanting those cells or tissues in the same individual during the same surgical procedure likewise do not require premarketing approval. In addition, federal regulations contain detailed criteria specifying when autologous or allogeneic cells can be used without first obtaining FDA premarketing approval. These criteria are identified in 21 CFR 1271.10. We mention these important sections of 21 CFR 1271 for a reason. Our goal was to identify businesses that engage in direct-to-consumer marketing of stem cell interventions and fit within our inclusion criteria. Judgments about regulatory compliance or noncompliance had no bearing on whether specific businesses were included in our database. Federal regulations governing marketing, manufacture, administration, and registration of cell-based interventions are complex, products are classified into different risk-based regulatory tiers, and we in no way wish to claim or imply that inclusion of particular businesses in Supplemental Table 1 means that they are noncompliant with federal regulations. Such determinations, as well as other assessments of regulatory compliance, must be made by legally authorized regulatory agencies after rigorous evaluation processes.

Organization and validation of Supplemental Table 1

Once U.S. businesses marketing stem cell interventions were identified that met these criteria they were listed in alphabetical order within Supplemental Table 1 and their websites were recorded. To provide documentation of our analysis company websites were downloaded and electronically archived using the Macintosh application SiteSucker. Next, content analysis of their websites was performed to collect data on companies' geographical location, the types of stem cells they market, the particular stem cell procedures they advertise, and the general disease and injury categories such businesses use to promote stem cell interventions. For example, some businesses promote stem cell interventions for neurological conditions and then list particular diseases such as ALS, Alzheimer's disease, and Parkinson's disease. During the initial search process as well as

subsequent data analysis phase we identified numerous businesses that use more than one name and have multiple websites. In such cases, we listed only what appeared to be the primary company names and websites.

Both researchers reviewed and validated primary data on all clinic websites as well as all information generated from website content analysis and entered into the dataset. This dual system of review was used to improve the overall accuracy of the dataset.

In instances where questions arose during the content analysis process, clinics were flagged for further review and discussion until consensus emerged concerning what data should be recorded or whether clinics should be removed from the database. In most cases further analysis of company websites enabled us to identify where individual businesses claim they are located, what kind of stem cells they purport to use, and what type of stem cell treatments and therapies they advertise. However, there were exceptions, such as when clinics advertised autologous stem cell therapies but did not identify whether cells were obtained from adipose tissue, bone marrow concentrate, or some other source.

Limitations of search strategy

Despite the considerable effort we put into searching for U.S. businesses marketing stem cell interventions, our search strategy had limitations. There is no independent and authoritative database of U.S. companies engaged in direct-to-consumer promotion of stem cell interventions. There is therefore no preexisting database or registry against which we could validate our findings. The search terms we used could have missed businesses using promotional words and phrases we failed to identify. "Selection bias" is built into the use of particular search phrases. We tried to address the problem of selection bias by using as many relevant search terms as possible, conducting searches on more than one search engine, and reviewing many pages of results rather than halting after the first few pages. However, it is possible that use of other search terms could have helped us identify additional businesses meeting inclusion and lacking exclusion criteria for our database. Use of "Google Alerts" is subject to the same kind of limitation. We also note that our searches were confined to English words and phrases. We acknowledge the possibility that our searches did not identify businesses marketing themselves using languages other than English.

Data analysis

Quantitative analyses of the data recorded in Supplemental Table 1 were conducted using both the search function within Google Docs as well as using formulas within Microsoft Excel. Data produced from the two methods were identical. The base Excel template formula we used was =COUNTIF(G3:G353, "*X*") where X was the text

being searched for in any given case. The search range (e.g. in this case G3:G353) was specified within the database depending on whether we were searching for stem cell types or conditions. To facilitate quantification, in addition to columns with full descriptive text on stem cell types and conditions, we also included separate parallel database columns with specific abbreviations that were then used as the basis for the formula-based analysis.

Stem Cell Type Abbreviations for Database Analysis

A = Amniotic stem cells

Allo= Unspecific allogeneic cells

BL = Blood stem cells including stem cells from peripheral blood

BM = Bone marrow related stem cells

D = Dental

ESC = Embryonic stem cells

F = Fat, adipose, and SVF

IPSC = IPSC

MSC = MSC if not specified as fat, marrow, etc.

P = Placental

U = Undefined

UCB = Umbilical Cord Blood cells

VSEL = Very Small Embryonic Stem Cell-Like Cells

X = Xenogeneic

Marketed Condition Abbreviations for Database Analysis

A = Aging, anti-aging, "rejuvenation", and telomere lengthening.

ALZ = Alzheimer's, dementia, cognitive impairment, senility, memory.

C = Cardiovascular including heart, stroke, ischemia, avascular necrosis.

Ca = Cancer.

Co = Cosmetics, aesthetics.

D = Diabetes along with any other metabolic conditions.

De = Dental, gum disease, other oral health conditions.

pD = Pediatric diabetes.

E = Ear, hearing issues.

F = Fatigue.

GI = Gastrointestinal issues including Crohn's disease & IBS.

H = Hair including alopecia.

Hep = Hepatic and liver conditions.

I = Immune, autoimmune including multiple sclerosis, HIV, other viral conditions, rheumatoid arthritis and other rheumatologic conditions.

INS = Insomnia, sleep issues.

K = Kidney.

L = Lung and other respiratory.

M = Muscular dystrophy, but not muscle tears, which are under O for Ortho.

N = Neurological including neurodegenerative conditions, neuralgia,

headaches, and concussion. Note that some conditions are both immunological and neurological.

N.D. = Not defined

O = Ortho including osteoarthritis conditions (but not rheumatoid arthritis), nerve pain, neuropathy, nerve injury, nerve entrapment and pinched nerves (but not neuralgia).

P = Pain

pN = Pediatric neurological (Autism, Cerebral Palsy, etc.)

S = "Sports" or "Sports Medicine" or an actual sport (e.g. Tennis, Golf) mentioned by name

SCI = Spinal Cord Injury and paralysis.

Sex = Sexual enhancement, erectile dysfunction, vaginal rejuvenation.

Sk = Skin including wound healing, scarring, radiation injury, and psoriasis.

Note that Lichen Sclerosis is both a skin and immune condition.

U = Urologic, not including purely kidney issues.

V = Vision and other optic conditions.

Production of the map

The map of the geographic data was made using the My Maps tool of Google Maps. The location data were imported into My Maps as an Excel spreadsheet. Only one city, Bal Harbour Islands, Florida, was not recognized by Google Maps and this location was therefore reassigned to the nearest major city of Miami Beach. Each city was assigned a red pin on the map, unless ≥ 10 businesses were present in a given city. In the latter case, such cities have been designated by one blue star each. These hot spot cities include Beverly Hills, Los Angeles, Phoenix, San Antonio, Austin, and New York. For each city with 1-9 businesses, only one pin is shown. There are a few stem cell businesses present in Hawaii and Alaska, but only the continental US is shown in order to retain map resolution. In the few instances when My Maps misidentified California cities as being located in Canada based on the CA geographic abbreviation, "California" was spelled out and used as the state identifier rather than using "CA".

Supplemental Figure 1. Maps of Metropolitan Areas with High Concentrations of Stem Cell Businesses Directly Marketing to Consumers

Based on the national map of our findings in Figure 1, we zoomed in on four metro areas that had relatively high numbers of businesses in our database. Each pin represents a city with at least one business in the database. Proceeding clockwise from top left, the metropolitan areas are: Southern California, Miami region, Dallas area, and Denver.

Limits of and context for analysis

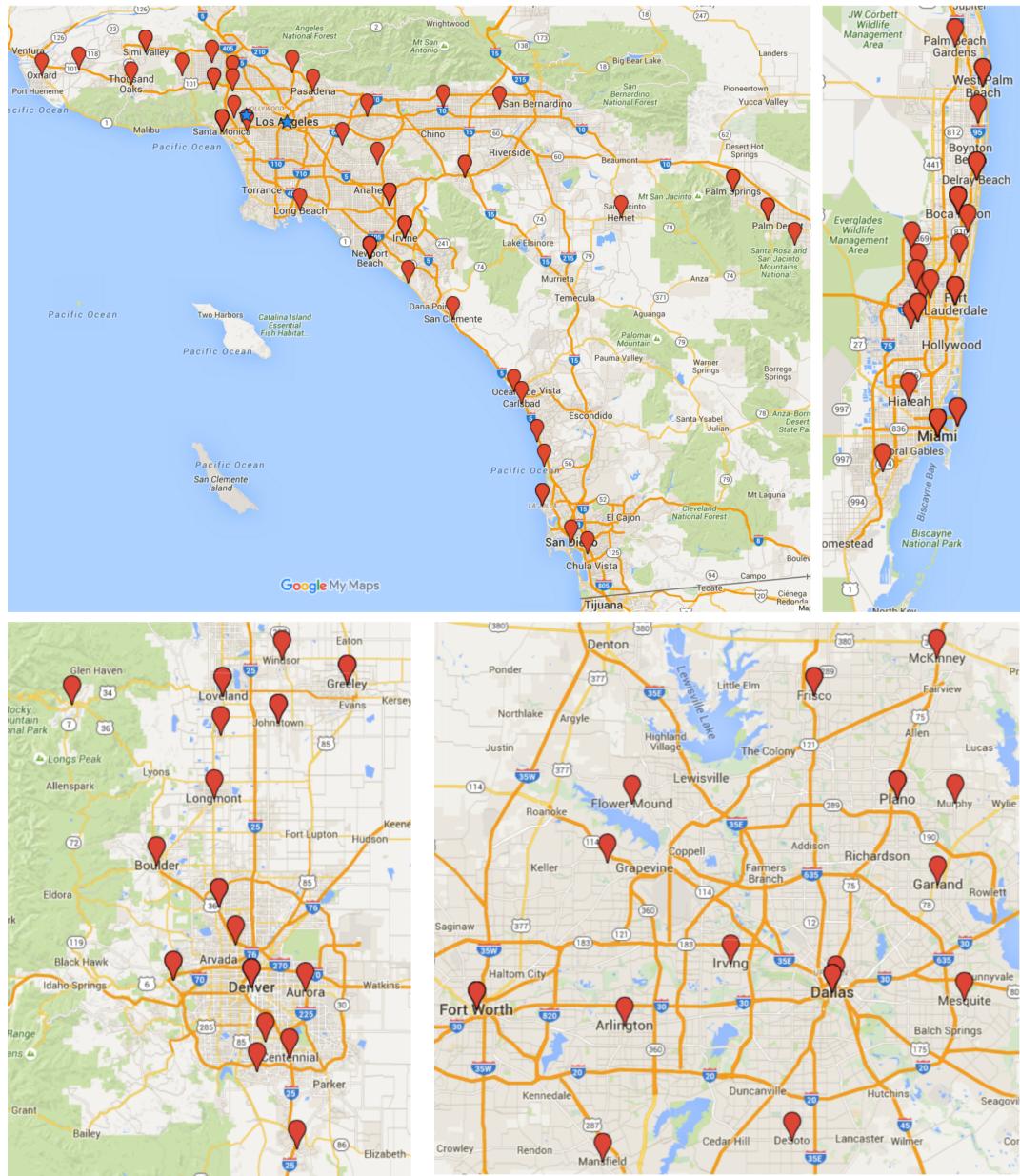
A key point must be made concerning the analysis of clinic websites. We investigated the marketing claims that businesses promoting stem cell procedures make to prospective clients. This method does not provide insight into the accuracy of such claims, address whether patients are in fact administered “stem cells” when they visit these facilities, or answer questions concerning the safety and efficacy of such interventions. What data mining and content analysis of clinic websites does provide is considerable insight into advertising claims. In some cases – such as when assertions are made about treatment of diseases and injuries for which approved, effective cell-based therapies do not yet exist – specific marketing claims ought to prompt discussion about whether particular U.S. based businesses are engaged in accurate advertising, administering cell-based interventions that in all respects comply with applicable state and federal laws and regulations, and have sufficient peer-reviewed scientific evidence of safety and efficacy to administer the stem cell “treatments” they market. We hope that our analysis of U.S. businesses marketing stem cell interventions directly to consumers contributes to such a public debate.

Search Terms Used to Find U.S.-Based Businesses Engaged in Direct-to-Consumer Marketing of Stem Cell Interventions

Adipose stem cell clinic
Adipose-derived stem cells clinic
Adipose stem cell therapy
Adipose stem cell therapy in the United States
Adipose stem cell therapy in the U.S.
Adipose stem cell treatment
Adipose stem cell treatment in the United States
Adipose stem cell treatment in the U.S.
Adipose stem center
ALS stem cell therapy
ALS stem cell treatment
American stem cell center
American stem cell clinic
Amniotic stem cell center
Amniotic stem cell therapy
Amniotic stem cell treatment
Amniotic stem cells treatment
Amniotic stem cells United States
Arthritis stem cell therapy
Arthritis stem cell treatment
Autism stem cell therapy
Autism stem cell treatment
Bone marrow derived stem cells

Bone marrow stem cell center
Bone marrow stem cell therapy
Bone marrow stem cell treatment
Cell Surgical Network
Cosmetic surgery clinic stem cells
Diabetes stem cell therapy
Diabetes stem cell treatment
Erectile dysfunction stem cell therapy
Erectile dysfunction stem cell treatment
Fat stem cell center
Fat stem cells
Fat-derived stem cell therapy
Fat-derived stem cells
Fat-derived stem cells treatment
Fat stem cell therapy
Fat stem cell treatment
FDA stem cell clinic United States
FDA stem cell therapy United States
FDA stem cell treatment United States
Institutional Review Board stem cells SVF
IRB SVF stem cell clinic
IRB SVF stem cell therapy
IRB SVF stem cell treatment
Multiple Sclerosis stem cell therapy
Multiple Sclerosis stem cell treatment
Pain stem cell therapy
Pain stem cell treatment
Paralysis stem cell therapy
Paralysis stem cell treatment
Placenta stem cells
Placental stem cells clinic
Regeneration stem cells United States
Regenerative medicine clinic
Regenerative medicine clinic stem cells
Regenerative medicine stem cells
Regenerative medicine stromal vascular fraction
Regenerative medicine SVF
Regenexx
Rejuvenate stem cells United States
Rejuvenation stem cells
Rejuvenation stem cells U.S.
Rejuvenation stem cells United States
Sports stem cell therapy
Sports stem cell treatment
Stem cell anti-aging treatment
Stem cell breast augmentation

Stem cell center
Stem cell clinic
Stem cell clinic California
Stem cell facelift
Stem cell injections knee
Stem cell regenerative medicine
Stem cell therapies
Stem cell therapies in the United States
Stem cell therapy
Stem cell therapy in the United States
Stem cell therapy in the U.S.
Stem cell treatment
Stem cell treatment in the United States
Stem cell treatment in the U.S.
Stem cell treatment for aging
Stem cell treatment for arthritis
Stem cell treatment for autism
Stem cell treatment for COPD
Stem cell treatment for Diabetes
Stem cell treatment for knees
Stem cell treatment for pain
Stem cell treatment for paralysis
Stem.MD
Stromal Vascular Fraction stem cell clinic
SVF stem cell clinic
United States stem cell clinic
U.S. stem cell clinic
U.S.A. stem cell clinic



Turner & Knoepfler, Supp. Figure 1