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## EVALUATION OF KNOWLEDGE ON INDUCED PLURIPOTENT STEM CELLS AMONG THE GENERAL POPULATION AND MEDICAL PROFESSIONALS

*ISPITIVANJE ZNANJA PRIPADNIKA OPŠTE POPULACIJE I POPULACIJE MEDICINSKIH RADNIKA O INDUKOVANIM PLURIPOTENTNIM MATIČNIM ĆELIJAMA*

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**Summary**
**Introduction.** Induced pluripotent stem cells are ethically much more acceptable than embryonic stem cells. The aim of this paper is to evaluate the knowledge on these cells among the general population and medical professionals, because this may influence further research. **Material and Methods**. We conducted a survey to assess knowledge on induced pluripotent stem cells among the general population and medical workers. The inclusion criteria were age over 18 years and the ability to read and write in Serbian. The survey was conducted via email and printed materials using a validated questionnaire for evaluation of awareness, knowledge, and attitudes towards donation, storage, and application of induced pluripotent stem cells. The collected data were entered into an Excel database, and complete statistical analysis was performed using the Statistical Package for the Social Sciences version 26.0. **Results**. The rate of correct answers among health workers ranged from 17.5% to 67.1%, and among the general population from 16.4% to 49.4%. The average number of correct answers per respondent in the population of health workers was 6, while in the general population it was 4, which is statistically significantly lower. **Conclusion**. The research results showed that healthcare workers have a higher level of knowledge on induced pluripotent stem cells than members of the general population, but the level of knowledge can be influenced by the level of education, availability of information, socioeconomic status, ideology, and conservative attitudes.
**Key words**: knowledge, induced pluripotent stem cells, general population, medical workers

**Sažetak**
**Uvod.** Indukovane pluripotentne matične ćelije su etički mnogo prihvatljivije od embrionalnih matičnih ćelija. Cilj ovog rada je da se ispita znanje pripadnika opšte populacije i populacije medicinskih radnika o ovim ćelijama jer to može uticati na dalja istraživanja. **Materijal i metode.** Sproveli smo anketiranje kako bismo procenili znanje između opšte populacije i populacije medicinskih radnika. Kriterijumi za uključivanje u studiju bili su da su ispitanici osobe starije od 18 godina i da imaju sposobnost čitanja i pisanja na srpskom jeziku. Istraživanje je sprovedeno korišćenjem validiranog Upitnika za procenu informisanosti, znanja i stavova o donaciji, skladištenju i primeni indukovanih pluripotentnih matičnih ćelija putem e-pošte i korišćenjem štampanih materijala. Prikupljeni podaci su prezentovani u *Excel* bazi podataka, a kompletna statistička analiza podataka izvršena je korišćenjem *IBM SPSS* softverskog paketa verzije 26.0. **Rezultati.** Stopa tačnih odgovora među zdravstvenim radnicima kretala se od 17,5% do 67,1%, a među pripadnicima opšte populacije od 16,4% do 49,4%. Prosečan broj tačnih odgovora po ispitaniku u populaciji zdravstvenih radnika bio je 6, dok je u grupi pripadnika opšte populacije bio 4, što je statistički značajno manje. **Zaključak.** Rezultati istraživanja pokazali su da zdravstveni radnici imaju viši nivo znanja od pripadnika opšte populacije, ali na nivo znanja mogu uticati stepen obrazovanja, dostupnost informacija, socioekonomski status, ideologija i konzervativni stavovi.
**Ključne reči:** znanje, indukovane pluripotentne matične ćelije, opšta populacija, medicinski radnici

### Introduction

Induced pluripotent stem cells (iPSCs) have become one of the most common topics in recent years, both among members of the general population and in the scientific community. The question is how much we actually know about iPSCs?

The iPSCs are a type of pluripotent stem cells that can be obtained by reprogramming adult somatic cells into a pluripotent state in vitro by inducing a forced expression of four transcription factors that are important for the maintenance of pluripotency [1–8]. Although these cells show a number of similarities with embryonic stem cells (ESCs), there are

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***Abbreviations***

iPSCs – induced pluripotent stem cells
ESCs – embryonic stem cells
SPSS – Statistical Package for the Social Sciences
OR – odds ratio

also significant differences between these two types of cells; in addition to morphological and functional differences, the one that stands out from the aspect of research and potential application is ethical acceptability, where iPSCs are significantly more acceptable than ESCs [8–11]. They offer opportunities for potential treatment of diseases and injuries, restoring functions, and drug testing [12–23]. Also, it should be noted that potential application of stem cells is associated with a risk of tumorigenesis [8, 23–26].

The aim of this paper is to examine the knowledge about iPSCs among the general population and medical professionals. Similar studies were performed and showed that the general public was familiar with the terms of stem cells, as well as that respondents showed a certain level of knowledge [27–37]. We also expected our respondents to show a certain level of knowledge, whereby we expected that health professionals would show a higher level of knowledge compared to the respondents from the general population. Due to the interest in this topic, it is very important to assess the knowledge of both members of the general population and the population of medical workers, because awareness and knowledge can influence the formation of positive attitudes and support for further research.

## Material and Methods

The study was conducted in the period from September 1, 2021 to January 1, 2022, and it was designed as a survey-based cohort study which examined the general population and the population of health workers using a validated Questionnaire for Evaluation of Awareness, Knowledge, and Attitudes towards Donation, Storage, and Application of iPSCs [38] via e-mail and directly using printed material. The obtained data were entered into an Excel database, followed by statistical analysis of data and summarized research results.

The research was conducted in a Serbian-speaking area, in the territory of Kragujevac and Belgrade. The inclusion criteria were age over 18 years and the ability to read and write in Serbian. The sampling was random; the independent variables were gender, age, religion, ideology, socioeconomic status, level of education, and the dependent variables were awareness and the level of knowledge about iPSCs. The study surveyed a total of 1,047 respondents, 46.5% of men and 53.5% of women. Respondents were mostly aged 31 to 60 years (85.4%).

Complete statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 26.0. Data were presented in the form of numbers (percentage). Statistical significance was tested by the Chi-square test for variables in the form of frequencies of individual categories. Continuous variables were presented as mean with standard deviation (SD) or median with interquartile range (according to the data distribution tested by the Kolmogorov-Smirnov test). The significance of the difference in continuous variables was tested by the Student T-test for independent causes or Mann-Whitney test; Kruskal-Wallis test was also used for variables that had three or more categories. The correlation was tasted by Spearman correlation, and the correlation strength was assessed as very strong ($r > 0.5$), strong (r 0.3 - 0.49) or weak ($r < 0.29$). In the prediction of the dependent variables with the help of independent variables, univariate and multivariate logistic regression was performed, and the results were presented as an odds ratio (OR) or cross OR with a 95% confidence interval. The statistical significance was set at $p < 0.05$.

## Results

*Respondents employed in health care system in relation to respondents from the general population*

Of all respondents, 35.4% were health workers, while significantly more were respondents from the general population, 64.6%. Among health care workers, there were significantly more males compared to the general population (53.9% vs. 42.5%), in which there were more females ($p < 0.001$). In the group of health workers, most were aged from 31 to 50 years (79.8%), while in the general population most were aged from 31 to 60 years (80.2%). In terms of education and socioeconomic status, in both examined groups, most had a higher education, i.e. a university degree, but there were significantly more persons with a doctoral degree among the health care workers compared to members of the general population (37.5% vs. 5.6%); also, health workers mostly had incomes over 100,000 dinars, while members of the general population mostly had 50,000 to 75,000 dinars. When asked whether their religion affected their decisions, 32.6% of health workers partially agreed with it, 25.1% disagreed, while 17.3% said that they absolutely agreed with it. On the other hand, in the general population, 25% partially agreed with it, 24.3% disagreed, and 16% did not agree with it at all (Chi-Square test; $p <0.001$). The majority of respondents in both groups stated that they had highly or partially liberal ideological views (health workers: 64.7% vs. general population: 60.6%) (Chi-Square test; $p = 0.007$). All health workers responded that they were informed about stem cells online, while members of the general population were informed predominantly online (77.4%), but also through newspapers and television. Both groups of respondents believe that this topic is given insufficient, little or very little attention in the media and only 8% of health workers believe that it is paid enough attention ($p < 0.001$).

There was a statistically significant difference in the distribution of answers between health workers and the general population. A higher percentage of health professionals have heard about iPSCs com-

pared to the general population (82.5% vs. 65.7%). Also, compared to the general population, health workers statistically more often believe that these cells can be used in the treatment of diabetes (57.4% vs. 38.8%). An interesting thing is that both groups are most likely to consent to treatment with these cells (> 50% in both groups). Both groups mostly believe that there are risks in the use of these cells, but 10% of the general population answered this question with ''I do not know''. Both groups believe (56%) that these cells can be used as a cure. Health workers are significantly more likely to believe that treatment with these cells is both ethically and morally justified (80.9%), while the general population has the same view in only 57.4% of cases; they also answered that they would store iPSCs in Serbia, while the general population answered that they would also store these cells in Serbia, but almost 30% of respondents would store these cells abroad. Healthcare professionals are significantly more likely to donate these cells compared to the general population (70.4% vs. 54.6%), and more likely to support research with these cells compared to the general population (54.7% vs. 40.2%). Healthcare workers are significantly more likely to agree with research related to cloning of human tissues and organs compared to the general population (69.6% vs. 62.3%), and they are significantly more often interested in learning about these cells compared to the general population (86.3% vs. 55%).

We found that there is a statistically significant difference in the distribution of answers to most questions between health workers and the general population. The rate of correct answers among health workers ranged from 17.5% to 67.1%. The rate of correct answers among health workers ranged from 17.5% to 67.1%, and the least correct answers were given about the characteristics of pluripotent stem cells: self-renewal, potency and differentiation. In the general population, the rate of correct answers ranged from 16.4% to 49.4%, and the least correct answers were given about the transcription factors included in Thomson's modification: Oct4, Sox2, Nanog, and Lin28. Interestingly, the rate of correct answers in the general population did not exceed 50% to any question, while more than 50% of correct answers were given by health professionals to 5 out of 12 questions. The general population had a higher rate of correct answers: IPSCs can differentiate only into the bone, cartilage, and fatty tissue cells; Characteristics of pluripotent stem cells are self-renewal, potency and differentiation; and Reprogramming of somatic cells to IPSCs is done using only the non-integrative method with micro-ribonucleic acid.

Our results showed that the average number of correct answers per respondent from the group of health workers was 6 (3 - 7) (data presented as median with interquartile range: 25 – 75), while in the group of the general population it was statistically significantly lower 4 (1.25 - 7) (Mann-Whitney test; $p < 0.001$). In regard to the minimum and maximum number of answers per respondent, we see that in the group of health workers there were none giving 10 correct answers, while in the general population this range was from zero to all 12 affected. It is important to note that the number of respondents with no correct answers was significantly higher in the general population compared to health workers (16.3% vs. 1.1%), and it is similar with one correct answer (8.7 % vs. 0.5%). However, there were 2.4% or 16 respondents, out of a total of 676, from the general population group with eleven or all twelve correct answers, while there were no such respondents among health professionals. From two to ten correct answers in almost all categories, there were more respondents among health workers compared to the general population.

*Correlation between the respondents' knowledge and other variables*

If a correlation is made between the overall knowledge score in the group of health professionals or in the general population, a statistically significant correlation is established (Spearman's rho = -0.191; $p < 0.001$). This shows that the score increases in the group of health workers, while it is lower in the general population. Although this is statistically significantly related, the correlation coefficient shows that this is still a weak correlation, so this significance should be observed with caution. There is also a significant correlation between age and level of education, so the overall score gets higher with age and higher level of education.

The correlation between the overall knowledge score regarding awareness of health professionals shows that there is a statistically significant association with some variables. On the other hand, all questions on awareness of the general population are statistically significantly related to the overall knowledge score.

Regarding the connection of awareness of health workers and socioeconomic status, religion, ideology and media attention in relation to iPSCs, it can be noticed that there is a strong connection between certain characteristics. Socioeconomic status and the question on the level of awareness are strongly related, which means that respondents with higher financial incomes stated that they would rather leave their cells abroad than in Serbia ($r = 0.479$). Respondents with more conservative attitudes are less likely to give a positive answer regarding the donation of iPSCs for the purpose of treatment ($r = 0.489$). There is also a strong correlation between the level of awareness and ideological attitudes, i.e. respondents with more conservative attitudes are less likely to be interested in learning more about iPSCs ($r = 0.393$). There is also a strong correlation between the level of awareness and media attention given to iPSCs, i.e. more health professionals stated that the more attention is paid to these cells, the less they agreed with research related to cloning human tissues and organs ($r = 0.388$).

In regard to the connection between the level of awareness of the general population with socioeco-

nomic status, religion, ideology and media attention to iPSCs, there is a strong connection between certain characteristics. Ideology and the level of awareness are strongly connected, i.e. respondents with more conservative attitudes are less likely to give a positive answer regarding the donation of these cells for the purpose of treatment ($r = 0.334$).

Regarding the correlation between knowledge and socioeconomic status, religion, ideology and media attention related to iPSCs, although there is a statistically significant correlation between individual variables, no strong correlation between examined variables was established in both groups of examinees.

*Predictors of respondents' knowledge*

If the total sum of correct answers is presented in a histogram, specifically for health workers, specifically for the general population, it is noticed that 5 correct answers represent the mean value and it is viewed as limited value. The total sum of 5 answers plus 5 below is unsatisfactory, while 6 or more correct answers are satisfactory. If we first cross the OR for the whole group, where the dependent variable is whether the respondents had 5 correct answers below or above, and the independent variable is the affiliation to health care group or the general population, we see that a significant value is obtained (Univariate logistic regression: OR = 0.573 (0.443 - 0.740); $p < 0.001$). That is, health workers were 1.74 times more likely to be in the group with a total knowledge score over 5 correct answers. Therefore, we looked at all predictions separately for these two subgroups of respondents.

A multivariate regression analysis shows predictiors regarding the knowledge of health workers, including ideologies, attention paid to this topic in the media, and issues of their awareness (Do you think iPSCs can be used to treat diabetes? Do you think there are risks when using iPSCs for treatment? Would you keep your iPSCs in the state cell bank in Serbia or abroad? Do you agree with the research on cloning human tissues and organs? This shows that the more conservative attitudes the respondents have, and the less attention is paid to this topic in the media, the better the knowledge expressed in the overall score. Awareness also shows that if respondents think that these cells can be used to treat diabetes, there are risks in using these cells for therapeutic purposes, and if they leave these cells for storage in Serbia, they have higher scores. It has also been shown that those who agreed with tests related to cloning of human cells and tissues are more likely to have a score above 5.

On the other hand, a prediction for the general population was made and it was shown by multivariate regression analysis that significant predictors are age, religiosity, how much attention is paid to this topic in the media and how someone is informed about this topic. For example: Have you heard about induced pluripotent stem cells so-called iPSCs? Do you think iPSCs can be used to treat diabetes? Would you agree to be treated by iPSCs? Do you think there are risks when using iPSCs for treatment? Would you keep your iPSCs in the state cell bank in Serbia or abroad? Do you support research with iPSCs? Do you agree with the research on cloning human tissues and organs? Are you interested in learning more about iPSCs? Older respondents, the less religious he is; more respondents are informed through newspapers and television and not through the Internet, and the less attention is paid to this topic in the media, they have better knowledge expressed by the overall score. Awareness shows that if respondents have heard of iPSCs, they have higher scores on the scale of knowledge. If respondents think that iPSCs can be used to treat diabetes, there are risks in using these cells for therapeutic purposes, and if they would agree to treatment using these cells, they are more likely to have a score above 5. If they left iPSCs abroad, respondents showed higher scores. It has also been shown that those who agree with trials related to human cell and tissue cloning, they would support research on these cells, and those who would be interested in learning more about these cells are more likely to have a score above 5.

## Discussion

Awareness and knowledge of iPSCs can significantly influence the formation of attitudes among the general population and health professionals, which can later be reflected in the course of further research in this area. That is why it is important to examine awareness and knowledge, because it has been shown that respondents who were better informed and have greater knowledge have more positive attitudes towards research in the field of stem cells.

Similar studies conducted in Japan over several years aimed to survey public opinion on iPSCs; the results of the study showed that the general population in Japan is well informed about iPSCs and that it supports further research with these cells [27–31].

A survey conducted in Malaysia in 2015 included 88 randomly selected nurses, showed that 92% of nurses in their final year of study had moderate knowledge of stem cells, and 8% had a high knowledge of stem cells [32]. A similar study was conducted in Saudi Arabia in 2015 and it included 53 nurses. The assessment of knowledge before testing showed poor knowledge in 30.2%, average knowledge in 62.3% and good knowledge in 7.5%. After testing, a noticeable improvement in knowledge was observed, with 80.8% of respondents showing good knowledge and 19.2% average knowledge [34]. In a study conducted by McCaughey et al., 91.5% of respondents believed they understood what was meant by "stem cells", and only 16.1% knew that their sample could be maintained indefinitely, 51.8% of respondents knew that they could differentiate into any other adult body cell [33]. Abouzeid MI et al., conducted a study in Egypt (2017 – 2018) including a sample of 42 nursing students. The study showed that the respondents had a satisfactory knowledge in the pre-test, and after the of the educational program the subsequent test showed an improvement of up to 90.5% [35]. The results of a study conducted in Iran (2019 – 2020) showed that the

knowledge of medical students from different years of study depended on the year of study, practice and period of externship periods. It is interesting that the participants showed the best knowledge of the use of stem cells, especially students who had close relatives with degenerative neurological diseases [36]. A study conducted in Saudi Arabia in 2021 included students of medicine and dentistry; 72.4% of respondents showed average knowledge of stem cells, and 23% showed a high level of knowledge, with a significant positive correlation between attitudes and knowledge [37].

In our study, if the total sum of correct answers is presented in a histogram for both populations, a limit value of 5 is obtained (below 5 - unsatisfactory, 6 and more correct answers - satisfactory value); in this regard, the rate of correct answers among health workers ranged from 17.5% to 67.1%, and among members of the general population it ranged from 16.4% to 49.4%. Our results showed that the average number of correct answers per respondent in the population of health workers was 6, while in the group of members of the general population it was 4, which is statistically significantly lower. The following predictors have been shown to influence the knowledge of health professionals: ideology, stem cell representation as a current topic in the media and information, i.e. if the media pay less attention to this topic, respondents with more conservative attitudes have better knowledge; in addition, if respondents think that these cells can be used for potential treatment of diabetes, there are risks associated with using these cells, and if they would leave their stem cells for storage in Serbia, then they have higher scores; also respondents who support research related to cloning of human tissues and organs may have a higher score.

The hypothesis that healthcare professionals have a higher level of knowledge about iPSCs compared to members of the general population was confirmed. However, this knowledge should be at an even higher level, given that professional literature is available to them, so future healthcare workers should be educated in more detail about these cells. In order to improve knowledge of the members of the general population about stem cells, especially about iPSCs, the level of information should be raised to a higher level, so it is necessary to inform the public better through social networks, video animations on potential applications and risks, organize educational programs that should be mandatory for members of medical profession, and which can be led by volunteers, final year students of medical and related universities.

## Conclusion

Based on the results of our research, we can conclude that health workers showed a higher level of awareness and knowledge about induced pluripotent stem cells compared to members of the general population, although awareness and knowledge, as shown by the results of our study, can be influenced by other factors such as ideology, conservative attitudes, availability of information, level of education and socioeconomic status.

Many researchers dealt with different topics, but had similar approaches to the problem by investigating the attitudes, awareness and knowledge of the public, which shows that the opinion of the public should not be ignored; the common conclusion is that it is necessary to enhance informative and educational strategies.

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