Від фундаментальних наук до клінічного застосування та серії симпозіумів: глобальне охоплення

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Поширення результатів дослідження серед науковців зазвичай відбувається через публікації оригінальних і оглядових статей у суворо контрольованих рецензованих наукових журналах. Безперечно, це вигідний і корисний спосіб спілкування, однак він не охоплює всіх потреб наукової взаємодії. Цей рукопис має на меті висвітлити незадоволену потребу в ефективному спілкуванні між науковцями під час міжнародних конфернецій і конгресів. У статті наведено коротку історію 35-річної серії симпозіумів «Міжнародні симпозіуми щодо ураження клітин-тканин і цитопротекції/органопротекції» (ISCTICO).

Ключові слова: наука, дослідження, міжнародне наукове спілкування, цитопротекція, ISCTICO.

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From basic sciences to clinical applications with a symposia series: A global outreach

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Dissemination of research results between scientists usually happens via publications of original papers & review articles published in strictly controlled, peer-reviewed scientific journals. This is certainly a beneficial and useful way of communication, but it does not cover all the needs in scientific interactions. This manuscript aims to highlight the unmet need for effective creative communication among scientists during international conferences and congresses. A brief history of the 35-years symposia series "International Symposia on Cell/Tissue Injury & Cytoprotection/Organoprotection" (ISCTICO) are presented.

Keywords: science, research, international scientific communication, cytoprotection, ISCTICO.

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Dissemination of research results between scientists usually happens via publications of original papers & review articles published in strictly controlled, peer-reviewed scientific journals. This is certainly a beneficial & useful way of communication, but it does not cover all the needs in scientific interactions. Namely, researchers often publish contradictory results, or they don't agree on the interpretation of certain data, e.g., disputes arise & often proliferate if not controlled or managed properly… A creative solution for this kind of problems is presented in this brief history.

In 1979, a stunning discovery was published in one of the best-controlled & most respected scientific journals in the field of gastroenterology, i.e., in Gastroenterology [1]. Namely, *Andre Robert*, MD, PhD (whom I knew personally, since he also obtained his PhD before me in the Institute of Hans Selye at the University of Montreal) described the prevention of chemically or drug-induced acute gastric erosions (or superficial bleeding ulcers) in rats pretreated with very low doses of prostaglandins (PG) that **did not** inhibit gastric acid secretion [1]. Since this was not a typical ulcer treatment or prevention, he called the new phenomenon "gastric cytoprotection" in the accompanied editorial in Gastroenterology [2]. This, almost unbelievable observation, created an uproar in the basic research & clinical gastrointestinal (GI) community. But very soon, not only new original publications appeared confirming the surprising results of Andre Robert (who worked at the Upjohn Pharmaceutical Company), but pretreatments of rats with very low doses (that didn't inhibit acid secretion), of other anti-ulcer drugs (e.g., cimetidine & probanthine) also inhibited the development of hemorrhagic gastric erosions induced by 100% (!) ethanol, very concentrated acid (HCl) or base (NaOH), or hot water…

Reading about these surprising results & coming from the institute of the 'father of stress' (at that time my research laboratory was in Boston at the Brigham & Women's Hospital/Harvard Medical School), I thought if so many drugs with very different structures & mechanism of action exert this "gastric cytoprotection" – there must be some nonspecific background in exerting their protection in the stomach, e.g., they may mobilize the antioxidant defense mechanisms in the stomach. Indeed, I was able to prove & publish in one of the best scientific journals in the world (Science) not only that pretreatment of rats with -SH containing chemicals like cysteine, N-acetylcysteine (Mucomyst), methionine prevents the chemically induced gastric lesions, but pretreatment of experimental animals with -SH alkylators (e.g., iodoacetamide, N-ethylmaleimide) abolished the protective effects of PG & other drugs [3]. This led to intensive disputes (often in front of the conference audience) with my old friend & colleague Andre Robert who argued about the supremacy of PG (e.g., that they protect by stimulating gastric mucus secretion, etc.)

Another interesting illustration of the non-specificity of gastroprotection (this term is now preferred over the misleading claim of total "gastric cytoprotection") [4] also originated from our lab, i.e., that gastroprotective drugs don't exert virtually any protection in adrenalectomized rats [5]. Thus, they work only in the presence of the active adrenal cortex, more specifically in the background of physiologic levels of endogenous glucocorticoids [5]. This observation has been greatly extended by subsequent investigations [6].

The initial discussions about the mechanisms of gastroprotection coincided with other disputes of two cell injury scientists who argued about the importance of intracellular calcium (*Sten Orrenius* at the Karolinska Institute in Stockholm, who later became chair of the Nobel Prize Committee) vs. the critical role of phospholipases in cell damage (*John Farber* at the University of Pennsylvania, Philadelphia, - who later became a co-author of one of the most modern & popular textbooks of pathology). Since I knew all these players personally, I proposed to them to have a few dedicated symposia where we could compare results & discuss their meaning in a friendly, professional atmosphere (fig. 1)… I also reminded my friends about the Greek origin of the word "symposium" (meaning 'eating & drinking party)… Around that time, another famous clinical investigator, *Klaus Henning Usadel*, professor of medicine at the University of Frankfurt in Germany)

International Symposia on Cell/Tissue Injury & Cytoprotection/Organoprotection (ISCTICO)

- *Originated from scientific disputes*:
- **Farber** vs. **Orrenius**: intracellular calcium vs. phospholipase activation in cell injury.
- **Robert** vs. **Szabo** (both Selye's students): prostaglandins vs. antioxidant sulfhydryls in "cytoprotection".
- **Usadel**: somatostatin & organoprotection.
- **Tarnawski**: sucralfate & antacids in gastroprotection.
- Many years later:
  - John Farber: Co-author of a very successful **Pathology Textbook**
  - **Sten Orrenius: Chair Nobel Prize in Medicine…**

Figure. 1. Main discoveries in cyto- and organoprotection

made another surprising discovery about the hepatoprotective, subsequently the gastroprotective effects of the 'paninhibitor' somatostatin. Hence, we also invited him to join our group & the 5 of us (i.e., *Robert, Szabo, Farber, Orrenius, Usadel*) became the founders of what we called "International Symposia on Cell/Tissue Injury & Cytoprotection/Organoprotection" (ISCTICO). The first meeting was organized in 1986 by Prof. Usadel in Heidelberg, Germany; the second one was organized by me in 1989 at Harvard Medical School. After moving to UCI, I organized two more events with the assistance of famous UCI gastroenterologist Prof. *Andy Tarnawski* (who replaced Andre Robert, after his untimely early death, in the Standing Committee of ISCTICO) in Long Beach, CA. Subsequently, symposia were organized in many countries of the world, many of these were attended by several Nobel Laureates as invited speakers. The most recent conference, the 11th ISCTICO was held in Pecs, Hungary in October, where I was invited to give two overview presentations: one as a co-founder about the origins of these conferences & one on the important role of early vascular injury in gastric mucosal injury & COVID-19 (fig. 2) [4, 5].

Another interesting aspect of this symposia series is the 'meeting of minds' in creativity in arts & sciences…Namely, when I organized this symposium in Boston in the 1980s, I tried to follow the example of my teacher & mentor Hans Selye. i.e., when he would organize a major symposium or conference,

International Symposia on Cell/Tissue Injury & Cytoprotection/Organoprotection

- **First**: Heidelberg, Germany, 1986; *K. H. Usadel*
- **Second**: Boston, MA, 1989; *S. Szabo*
- **Third**: Long Beach/Irvine, CA, 2000; *S. Szabo*
- **Fourth**: Long Beach/Irvine, CA, 2006; *S. Szabo & A. Tarnawski*
- **Fifth**: Yalta, Crimea, Ukraine, 2008; *T. Beregova*
- **6th**: St. Petersburg, Russia, 2011; *L. Filaretova*
- **7th** : Honolulu, Hawaii, USA; 2012; *K. Takeuchi*
- **8th:** Budapest, Hungary, 2014; *K. Gyires*
- **9th:** Krakow, Poland, 2016; *T. Brzozowski*
- **10th:** Kyoto, Japan, 2018; *K. Takeuchi*
- **11th:** Pécs, Hungary 2021; *Zs. Helyes, K. Gyires*

Figure 2. List of symposiums from 1986-2021

he asked famous artists to dedicate a panting or lithograph to his symposium. Probably the most famous contributor was Salvador Dali who dedicated a famous, new illustration of stress to the last symposium Selye organized: the 2nd Symposium on Stress Management in 1979 in Monte Carlo (fig. 3 left). Thus, when I organized my first conferences & symposia at Harvard, I wrote to Victor Vasarely, the founder of 'op-art', citing the experience of Hans Selye with Salvador Dali… I was just a young assistant professor at Harvard Medical School & I thought Vasarely would never reply to me, but within about a week I received 12 (!) original black & white lithographs with the note, essentially saying 'I am not sure what would fit your symposium, you should choose the best fit'… Well, I selected this (fig. 3 right) since it illustrates the many pathways' cells can be injured & also protected by various mechanisms:

The take-home message for young investigators is that if you were challenged or your results don't agree with others, don't argue, invite other colleagues, try to find a neutral ground, e.g., at special sessions at international conferences & congresses. Anybody interested in the more detailed history of ISTICO, please look at my book chapter on this topic, published a few years ago [6]. The bottom line: make friends, not enemies!

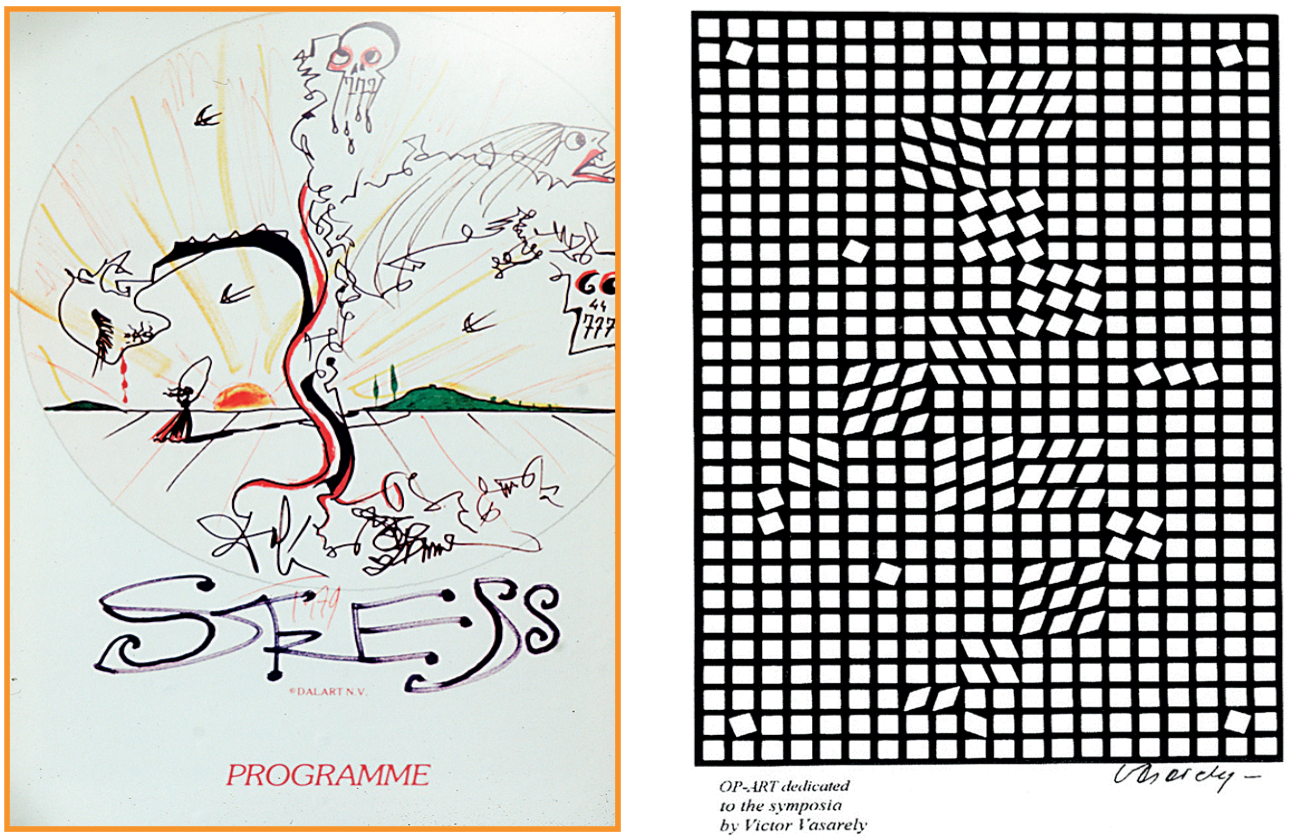

Figure 3. Salvador Dali (left) and Victor Vasarely (right) art works dedicated stress and cytoprotection

References

1. Robert et al. Prostaglandins (PG) prevent gastric necrosis produced by alcohol, HCl, NaOH, hypertonic NaCl & thermal injury. *Gastroenterology*,1979, 77, 433-443.
2. Robert A. Cytoprotection by prostaglandins. *Gastroenterology,* 1979, 77, 761-767.
3. Szabo S, Trier JS, Frankel PW. Sulfhydryl compounds may mediate cytoprotection. *Science* 1981; 214:200-202.
4. Szabo S, Szelenyi I. Cytoprotection in gastrointestinal pharmacology. *Trends in Pharmacol. Sci*., 1987, 8, 149-154.
5. Szabo S, Gallagher G, Horner HC, Frankel PW, Underwood RH, Konturek SJ, Brzozowski T, Trier JS. Role of the adrenal cortex in gastric mucosal protection by prostaglandins, sulfhydryls and cimetidine in the rat. *Gastroenterology* 1983, 85, 1384-1390.
6. Filaretova L. Glucocorticoids are gastroprotective under physiologic conditions. Ther Adv Chronic Dis, 2011, 2(5), 333-42.
7. Szabo S. The origins of ISCTICO: From scientific disputes to professional friendships. *Proc. of 11th ISCTICO*, Pecs, Hungary, 2021. https://huphar.org/isctico2021/
8. Szabo S. The origins of ISCTICO: Vascular endothelial injury: Common element in the cellular & molecular pathogenesis of GI ulceration & COVID-19. *Proc. of 11th ISCTICO*, Pecs, Hungary, 2021. https://huphar.org/isctico2021/
9. Szabo S, Tache Y, Tarnawski A. The 'gastric cytoprotection' concept of Andre Robert and the origins of a new series of international symposia. In: Filaretova LP, Takeuchi K (eds.): *Cell/Tissue Injury and Cytoprotection/Organoprotection in the Gastrointestinal Tract: Mechanisms, Prevention and Treatment. Frontiers of Gastrointestinal Research*. Basel, Karger, 2012, 30, 1–23.