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Excessive exuberance in press reports of repurposed drugs with anti-COVID-19 efficacy

Cuba's "medical miracles" the most egregious

The irresponsibility of those who would promote the unfounded efficacy of interferon alpha 2b (IFN α 2b) in treating COVID-19, a story that has hit the internet and carried in recognized newspapers⁽⁺⁾ in the past few days as being Cuba's unique, prospective therapeutic, joint ventured with China, is staggering! That the author of the LSE column "***Cuba and coronavirus: how Cuban biotech came to combat COVID-19***"* further failed to describe its risk of possibly pernicious** effects questions aspects of the motive for the column.

The LSE paper by Helen Yaffe, on which this report concentrates, is just one in an outpouring of regrettable and dangerous information about prospective therapeutics. Not all relate to Cuba – repurposed drugs from Japan, Europe and the US also the stuff of speculation – but many of these are attributed to Cuba's mythical excellence in bio therapeutics. Amongst the most dangerous are:

"BioCubaPharma⁽⁺⁾ guarantees production of 22 medications for the treatment of Covid-19"*** and ***"How Cuba is Leading the World in the Fight Against Coronavirus"*******

Even the insinuation, as Yaffe writes in the LSE article, that this 1950's drug is somehow novel, even though ubiquitous for decades, is monstrous. She adds for attestation "... [from Cuba's] now world-leading biotech industry" – a statement that is knowingly distant from veracity. Notwithstanding a devoted, intelligent and highly-informed scientific community in Cuba, its establishment by Fidel's salutary and foresightful initiative, massive investment by its government, its amazing achievements given its inability to access to the flood of biocapital in the rest of the world, output from the Polo Científico has *never* been "world-leading."

Interferon is not a "Cuban drug" nor is it new. It was first described - and named - in 1957 by Isaacs and Lindenmann at the National Research Council in the UK. Interferons became a cornerstone of the Cuban biopharmaceutical strategy that Fidel initiated in the '80s — in which interferon development was made possible by R. Lee Clark (not Clark Lee as Yaffe writes), the then president of MD Anderson, who made the technology available to Cuba.

If there is one thing that Cuba does well – exceptionally well – it is that of being opportunistic and has demonstrated considerable success through a cadre of Cubaphiles, principally in the US and the UK, continuing to extol the virtues of a range of purportedly exceptional therapeutics.

Notwithstanding this following of adherents, it remains, that YM BioSciences was, and remained until just ~a year ago, the only organization in that country's *entire history* that actually treated patients in major-market countries with a Cuban-origin drug, and for which it was the first to achieve FDA clearance. The author of this note was the chairman and chief executive of YM BioSciences.

The Kool-Aid drinkers have never, yet, been able to follow-through with their sycophantic views of what is, sadly, given the selfless dedication of the members of its scientific community, a broken business by actually identifying any product of utility for human health translated from Cuba's many biopharmaceutical initiatives in any major market country. Yes, there are joint ventures in China, but I have grave doubts that production of anything other than generic interferon and a benign, but marginally-effective, EGFR monoclonal antibody, has made a mark. Indeed, "*generics*" is precisely what the Cuban pharmaceutical establishment is good at and on which it should be concentrating.

The story of Cuba's exceptional earlier achievements in biopharmaceuticals is here: <https://www.cubanbiotec.com/thesagaofcubanbiosciences> and, in depth, here:

The Cuban Cure: Reason and Resistance in Global Science – S.M. Reid-Henry, U of Chicago Press 2010

Cuban interferon (and the Chinese-manufactured version under Cuban guidance) is a generic product, not functionally dissimilar to generic IFN manufactured by a whole range of companies all over the world. The initial developer was Biogen that licensed it to Schering in 1979. There are now umpty-ump companies, including Merck and Teva.

The mechanism of action of interferons is not specifically directed to the virus; but as a cytokine that participates in the process of defense against viral replication, proliferative disorders, etc. As I understand it from the limited amount of currently available clinical data, efficacy of IFN α 2b in Chinese patients is marginal-to-absent (<https://doi.org/10.1517/14712598.4.6.827>) even though interferons have been used in the management of previous respiratory infections epidemics, such as influenza and SARS, the latter which is also a coronavirus. I am not aware that interferons have been utilized as a "*first line*" therapeutic anywhere. Again, the mechanism is non-specific, and IFNs have no direct antiviral effect. Thus it is even more disconcerting that Yaffe selectively quotes Cuba's Center for Genetic Engineering and Biotechnology's (CIGB), Dr. Luis Herrera, as saying "*its use prevents aggravation and complications in patients, reaching that stage that can ultimately result in death*", deliberately intimating a connection between Cuba's generic IFN α 2b and COVID-19. Herrera, however, is not blameless, reportedly stating that the drug has "*proven effective for viruses with characteristics similar to those of COVID-19.*" This is sheer irresponsibility – there is no evidence that COVID-19 is similar to other coronaviruses.

With Cuba and its acolytes reportedly claiming that Chinese data supports the use of IFN α in coronaviruses the limited amount of currently-visible Chinese clinical data regarding its efficacy, has, so far, demonstrated its efficacy to be marginal to absent. That of which we are aware is that conducted by Zhao Z, Zhang F, et al in 2003*****

Both Yaffe and Herrera would be aware that there is considerable uncertainty regarding interferons as they affect certain coronaviruses. More importantly, the Abstract from the paper** I quote immediately below further describes severe negative effects of interferons in SARS-coronavirus.

While that does not necessarily mean that the increased harm observed in that study is certain to occur with the COVID-19 coronavirus, it would importantly question the dubious effort to attempt to link Cuba's purported efficacy of IFN α 2b in the present case, and sufficient to discourage one to use it – *"The imbalance in the [interferon] response is thought to contribute to the establishment of viremia early in infection, whereas the production of chemokines by infected organs may be responsible for (i) massive immune cell infiltrations found in the lungs of SARS victims, and (ii) the dysregulation of adaptive immunity"*. What this conclusion specifically does, however, is to repudiate Herrera's statement about "similar" coronaviruses.

And, to take it one step further, the public claims by CIGB regarding the Cuban's efficacy in Dengue and HIV-AIDS are, themselves, subject to considerable doubt and lack supporting evidence. Is interferon, let alone Cuba's IFN α 2b, broadly prescribed elsewhere for those conditions that are hardly limited to Cuba?

Cuba, as it has done with many of its now quite-dated drugs – as is IFN α 2b – is using the current societal disaster to draw publicity and sympathy to itself while profiling purported achievement against the COVID-19 pandemic; but its biopharmaceutical establishment is no longer at the cutting edge that it was at when we, at YM BioSciences, became directly involved with it at the request of the Cuban Government, 25 years ago. It is, equally, contradictory that what is internationally recognized as the best and most necessary methods of control – quarantine and self-isolation – is in stark contrast to what the Cuban Government has been doing – keeping borders open, schools operating, no quarantine or self-isolation. This, in the context of the absence of the essentials to alleviate risk and consequences – soap, sanitizers, toilet paper – already scarce in Cuba and adding more weight to the day-to-day burdens of its citizens. As just one example, recognizable to those familiar with Cuba, a typical taxi in Havana is a car from 1940-50's shared with six passengers and a driver.

The voices of praise outside of the country for the marvels of Cuban biopharmaceuticals are frequently hyperbolic and, regrettably, often in contrast to the data. One of many examples is Helen Yaffe being quoted as saying that Cuban biopharmaceuticals are *"world-leading"*. Cuba's efforts are admirable, but the Polo Cientifico is not in the first league. And claiming efficacy in coronaviruses with *"... an antiviral that boosts the human immune system"*, implying efficacy in COVID-19 is prospectively harmful and contrary to the risks suggested by the German trial highlighted above that concludes with the drug specifically causing *".....dysregulation of adaptive immunity."* The hyperbole is dangerous and irresponsible.

Yes, there is still a huge investment from the Cuban government supporting what is largely a failed business; and this on top of the monster economic and societal issues that that country has to deal with. Notwithstanding its scientific community there has been nothing new of consequence in Cuban medical product development since its launching of cancer-targeting MAbs in the 1990s - and to laud the 1980's generic interferon as a COVID-19 solution is morally reprehensible.

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<https://www.cresswelladvisors.com/leadership>

+ The UK's Guardian/Observer, Irish Mirror, the US's The Nation & Newsweek, India's The Telegraph & The Week

REFERENCES:

* <https://blogs.lse.ac.uk/latamcaribbean/2020/03/18/cuba-and-coronavirus-how-cuban-biotech-came-to-combat-covid-19/>

** Interferon and Cytokine Responses to SARS-Coronavirus Infection. Volker Thiel , Friedemann Weber - Cytokine & Growth Factor Reviews 19 (2008) 121–132 -

<https://www.sciencedirect.com/science/article/pii/S1359610108000026>

** *<https://jamaicapeacecouncil.wordpress.com/2020/03/20/biocubapharma-guarantees-production-of-22-medications-for-the-treatment-of-covid-19/>

****<https://www.mintpressnews.com/cuba-leading-world-fight-against-coronavirus/265771/>

***** *Role of interferons in the treatment of severe acute respiratory syndrome.* Jindrich Cinatl Jr, Martin Michaelis, Martin Scholz & Hans Wilhelm Doerr – <https://doi.org/10.1517/14712598.4.6.827> (download PDF)

+ +Actually, BioCubaFarma – but this inaccuracy merely mirrors much of the content

POST 2020-03-22 NEWS

This report on the announcement of the launch of a global megatrial by WHO could, in one of its arms, lead to a sound conclusion about the value of IFN for the treatment of COVID-19.

<https://www.sciencemag.org/news/2020/03/who-launches-global-megatrial-four-most-promising-coronavirus-treatments>

Notice the comment in the paragraph describing this arm: *"The use of interferon-beta on patients with severe COVID-19 might be risky." "If it is given late in the disease it could easily lead to worse tissue damage instead of helping patients"*

A common finding in these three articles - below - is that IFN does not appear to have been either efficacious or safe in patients at advanced stages. These reports reflect **actual treatment** of coronavirus patients (not COVID-19).



Rivabirin plus
interferon 2014.pdf



Rivabirin plus
interferon 2013.pdf



Interferons and
coronavirus 2015.pdf

1. J Antimicrob Chemother 2015; 70: 2129–2132 IFN-a2a or IFN-b1a in combination with ribavirin to treat Middle East respiratory syndrome coronavirus pneumonia: a retrospective study.
2. IJID -9 December 2013- Ribavirin and interferon therapy in patients infected with the Middle East respiratory syndrome coronavirus: an observational study
3. Lancet Infect Dis 2014; 14: 1090–95 - Ribavirin and interferon alfa-2a for severe Middle East respiratory syndrome coronavirus infection: a retrospective cohort study